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VOLUME 96 April, 1953 NUMBER 4

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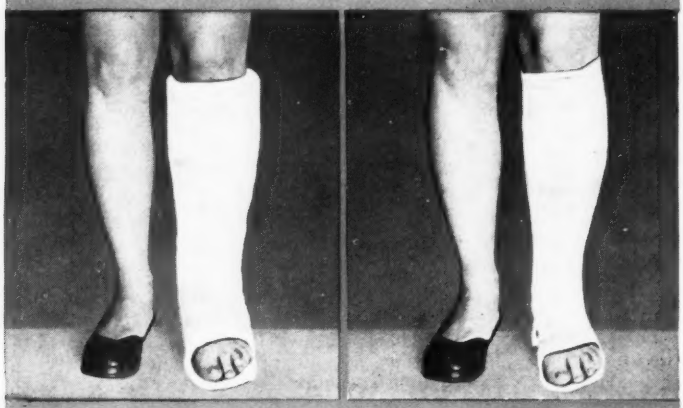

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references:

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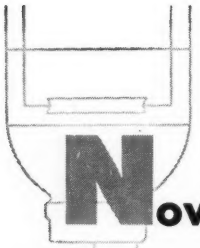

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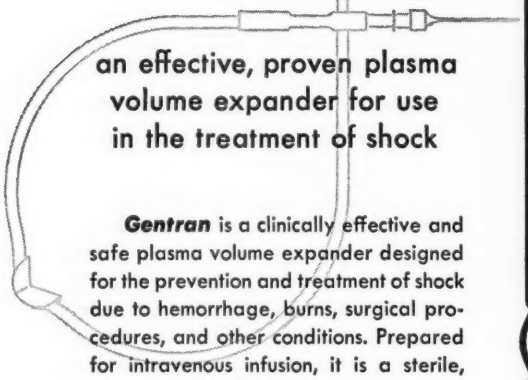

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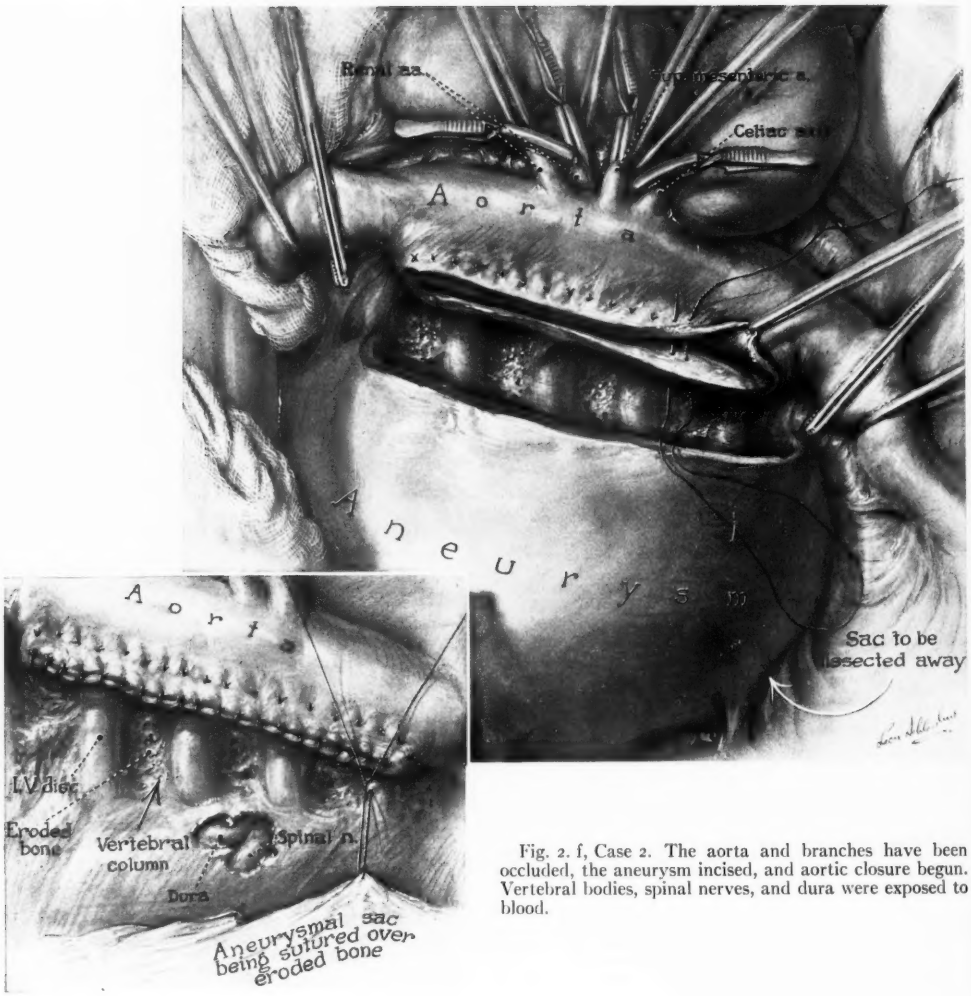


Fig. 2. f, Case 2. The aorta and branches have been occluded, the aneurysm incised, and aortic closure begun. Vertebral bodies, spinal nerves, and dura were exposed to blood.

Definitive Treatment of Saccular Aneurysms of the Aorta with Excision of Sac and Aortic Suture.—Henry T. Bahnson.

SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 96 APRIL, 1953 NUMBER 4

DEFINITIVE TREATMENT OF SACCULAR ANEURYSMS OF THE AORTA WITH EXCISION OF SAC AND AORTIC SUTURE

HENRY T. BAHNSON, M.D., Baltimore, Maryland

SINCE 1719, when Valisnari diagnosed an abdominal aneurysm and a surgeon described as unskillful lanced the tumor (1), aneurysm of the aorta has remained a major surgical problem. Many and varied forms of treatment have been advocated, and in some instances successfully used, although often they were little more than nonspecific remedies.

For saccular aortic aneurysm only two methods of treatment are currently in common use; namely, intrasaccular wiring and the employment of fibrogenic or reinforcing materials. The former method, although beneficial to many patients in its most refined form, requires wire which, because of its special insulation, is no longer available and special apparatus. Without this refined technique results have been less good. Wrapping with cellophane has given good results in isolated instances, but in a large series this technique has been helpful as palliation in only 40 per cent of the patients.

Although excision is an established method of treatment for aneurysms of peripheral arteries, it has been applied to aortic aneurysms only in isolated instances. When possible, excision of the sac and preservation of aortic continuity constitute the ideal treatment. Removal of the aneurysm relieves symptoms arising from pressure on nerves or adjacent, possibly vital, structures, and avoids later dissection or rupture. The following case reports establish the fact that saccular aneurysms of large or small size can be excised from all regions of the aorta with preservation of aortic continuity.

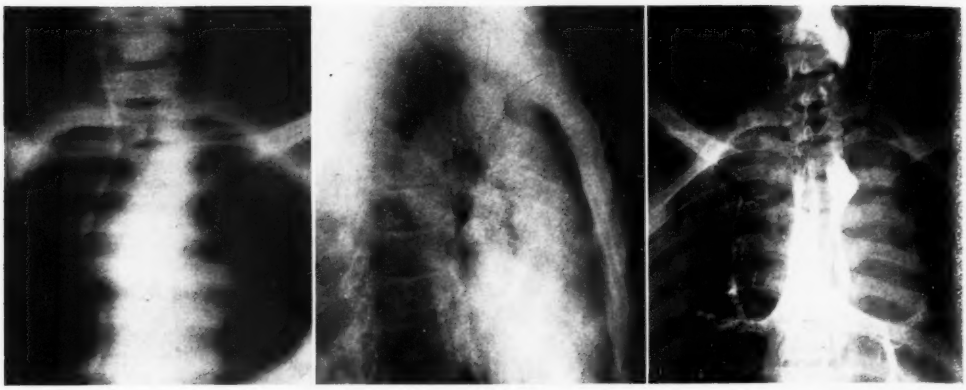
From the Department of Surgery, Johns Hopkins Hospital and University, Baltimore. The author is a John and Mary R. Markle Scholar.

CASE REPORTS

CASE 1. L. P., a 46 year old colored male, was seen because of shortness of breath and a wheeze of 4 months' duration. A dry cough, occasionally productive of blood, appeared soon after the initial symptoms. Dyspnea increased, kept him from working, and was bothersome when at rest. He had noted some malaise and weakness and had lost 34 pounds in 4 months. One month prior to entry he had been hospitalized elsewhere, and bronchoscopy had showed an extrinsic lesion with normal mucosa on biopsy. No history could be obtained of primary syphilis. He had received injections during 2 weeks for "bad blood" 7 years previously.

On admission he was poorly nourished and dyspneic at rest, with a nonproductive cough and occasional wheeze. No abnormality of heart and peripheral vessels was noted. Blood pressure was 120/80. Serological tests for syphilis were positive.

On tracheoscopy there appeared to be an extrinsic mass on the left anterior aspect almost occluding the trachea 7 centimeters below the glottis. A 7 millimeter bronchoscope could not be passed beyond the obstruction. Later, just prior to anesthesia, a 5 millimeter instrument was passed snugly. Esophagoscopy was normal.



a b c

Fig. 1. Case 1. A 46 year old man with a small but embarrassingly located aneurysm of the distal part of the aortic arch sought relief of respiratory obstruction. Excision of the saccular aneurysm and aortic suture were possible and the patient is well. a, Laminagram shows displacement to the right and extreme compression of the trachea by aneurysm of aortic arch. b, Angiocardiogram by Dr. Robert Sloan showing small but strategically located aneurysm of aortic arch. The ascending aorta is slightly enlarged; the aorta elsewhere is normal. c, Visualization of trachea and esophagus 2 weeks after operation showing normal size and position of the respective structures.

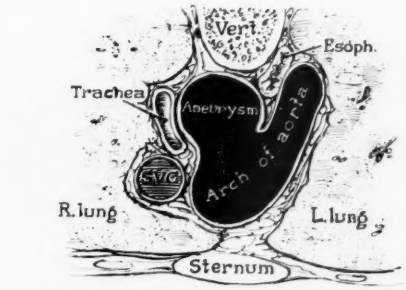
Roentgenologic examinations demonstrated slight widening of the upper mediastinum. On laminagraphy extreme narrowing of the trachea by pressure from the left was seen in the region of the aorta (Fig. 1a). Angiocardiography showed the small but embarrassingly located aneurysm of aortic arch (Fig. 1b).

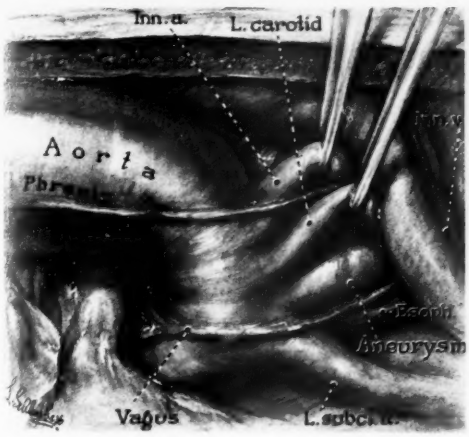
Operation was performed on February 6, 1952. Under local pontocaine Dr. Donald F. Proctor, who gave the anesthesia, visualized the tracheal obstruction and elected to administer the general anesthetic with a tracheal tube to, but not through, the constricted area. It was not necessary later to advance the tracheal tube. Thoracotomy was done through the second left interspace and the sternum was split from this level to the suprasternal notch. This gave good exposure. The aneurysm arose from the medial portion of the aortic arch behind the left common carotid, just proximal to the origin of the left subclavian artery (Fig. 1c). The great vessels, aortic arch, and neck of the sac were freed by dissection. After control of the aortic arch and great vessels was obtained the left subclavian artery was divided distally. A curved Gross coarctation clamp was placed across the base of the aneurysm and aortic arch, and the aneurysm was incised. The base of the aneurysm was closed, Halsted intestinal needles being used with interrupted No. 0000 silk in an attempt to make a normal aortic lumen (Fig. 1d). A two layer closure was performed by the use of mattress sutures proximally and overhand sutures distally. The suture line was approximately 8 centimeters long. When the clamp was removed slight bleeding was easily controlled. The aneurysmal sac was excised. The wall of the sac was fused to the trachea and the flattened cartilages were in direct contact with blood and clot. Apparently rupture had been imminent.

He had considerable respiratory difficulty for several days. Forty-eight hours after operation bronchoscopy showed a profuse thin discharge. The trachea was still flattened in the region of the aortic arch and the overlying mucosa was edematous. After tracheostomy and frequent suctioning he improved rapidly and his subsequent course was uneventful. Visualization of trachea and esophagus 2 weeks later showed normal lumen and position (Fig. 1e). Ten weeks after operation he was well, beginning to regain his lost weight, and ready to return to work. He was well 6 months later on last report.

Summary. A relatively young man with a small but embarrassingly located aneurysm of the distal part of the aortic arch sought relief of respiratory obstruction. Excision of the saccular aneurysm and aortic suture were possible and the patient is well. It was feared that wiring or the use of fibrogenic substances for aneurysm in this location would lead to local edema and further tracheal obstruction. Sloan and Cowley circumvented this danger by performing a posterior mediastinal tracheotomy. In order to avoid this sizable procedure and to treat the aneurysm definitively, resection seemed the ideal procedure. Scar tissue about the aneurysm safeguarded occlusion with a clamp and strengthened the repair, and little difficulty was encountered in suturing the aorta after division of the base of the aneurysm. Further use of this method seemed advisable.

Case 2. M. T., a 45 year old colored male, was struck by an automobile in May, 1950, and suffered injury to his back and left flank. He remained in bed at home for 6 months prior to a spinal fusion for a possibly mistaken diagnosis of tuberculosis. Pain and tenderness persisted, and he was admitted to this hospital in May, 1951, after a mass appeared in the





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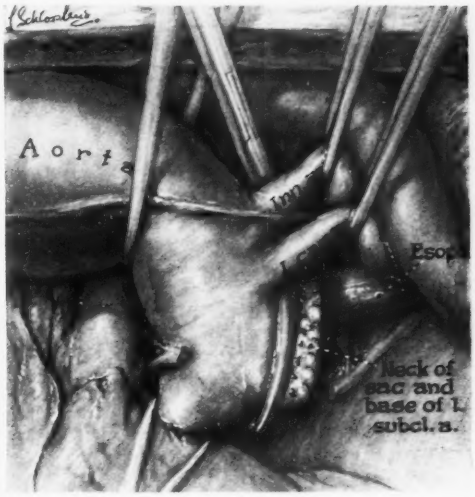


d

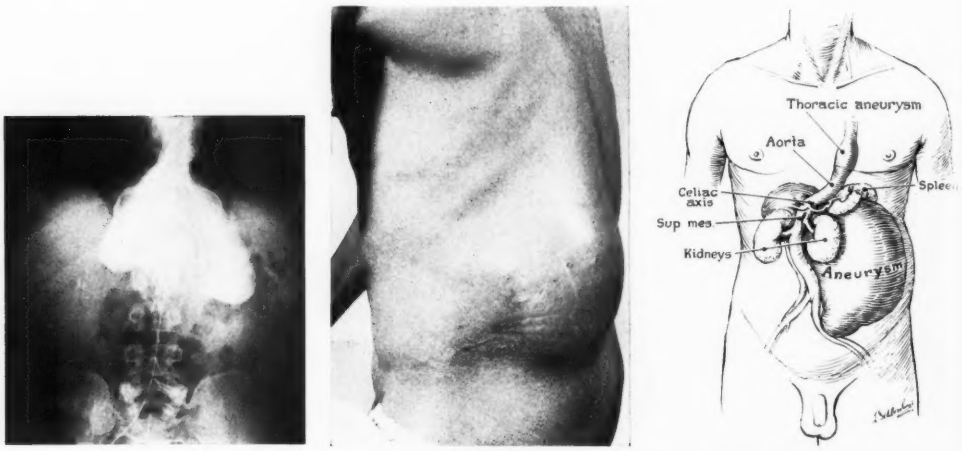
Fig. 1. c, Case 1. Cross section shows aneurysm arising from aortic arch compressing the trachea. Lower drawing illustrates the base of the aneurysm on the medial side of the aortic arch. Exposure is through the second left interspace and split sternum. d, The aneurysm and left subclavian artery have been excised after occlusion of the convexity of the aortic arch by Gross coarctation clamp. Two rows of interrupted silk sutures were used to close the aorta.

left costovertebral angle. No history of previous venereal disease could be elicited.

Serological tests for syphilis were positive. Aortography with a catheter passed retrograde by Dr. Willard Goodwin showed a lobulated upper abdominal aneurysm (Fig. 2a). Review of old and current roentgenograms of the lumbar spine showed changes consistent with the diagnosis of aneurysm, although an infectious process in the bodies of the first and second lumbar vertebrae could not be excluded. Transverse processes were absent on the second and third lumbar vertebrae. He was given penicillin therapy for late syphilis.

In June, 1951, five 10 meter segments of wire obtained from Dr. Arthur Blakemore were inserted on 2 occasions according to his technique. The last heating required 3.7 amperes and only serum could be obtained on aspirating the mass, indicating massive clotting. The patient was relieved of the pain in his back and was improved until January, 1952, when pain recurred with radiation down the left anterior thigh. A mass appeared in the abdomen and back and rapidly enlarged. He was admitted 2 weeks later. There was a tense pulsating mass in the left flank and abdomen (Fig. 2b) which was encroaching upon the costal margin above and the iliac crest below (Fig. 2c). An aortogram showed considerable enlargement of the aneurysm with spreading of the wire and a thick walled, soft tissue mass representing clot (Fig. 2d). Percutaneous wiring was performed by Dr. Glenn Morrow, using 10 meters of Blakemore wire and 300 feet of No. 32 stainless steel. Again only serum could be aspirated. The patient obtained considerable relief of pain but the mass seemed to enlarge, and on March 4, 1952, the aneurysm was excised.

A thoracoabdominal incision was made through the bed of the tenth rib. All the abdominal viscera and the aorta were found displaced forward and to the right by a large aortic aneurysm (Fig. 2e). The aneurysm extended upward to elevate both right and left diaphragmatic leaves. The mouth of the aneurysm appeared to extend from posterior to the origin of the celiac axis to the level of the renal arteries, a distance of 12 to 15 centimeters. These vessels and the aorta proximally and distally were isolated and temporarily occluded. The aneurysm was incised along its mouth, a cuff being left on the aorta for closure. A row of interrupted mattress sutures of No. 0000 silk on short Halsted intestinal needles was



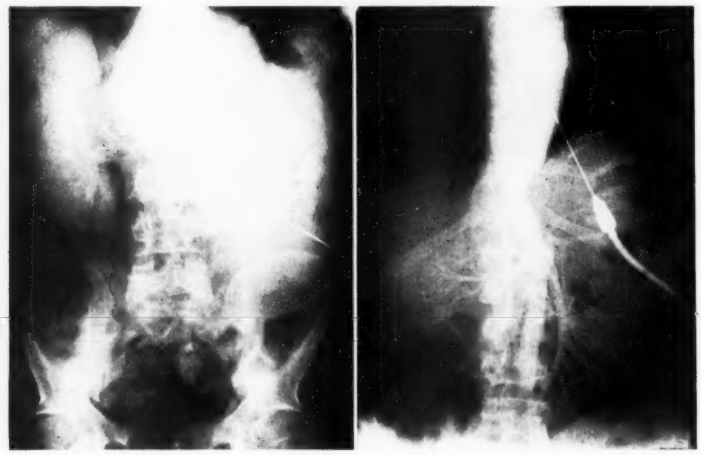


Fig. 2. Case 2. A 45 year old man with a saccular aneurysm of the upper abdominal aorta. In spite of 2 apparently satisfactory wiring procedures at an 8 month interval the aneurysm continued to enlarge. Regardless of the large size, the aorta could be controlled proximally and distally and excision performed with aortic restoration. a, Aortogram by catheter inserted retrograde through femoral artery. A bilobate saccular aneurysm of the upper abdominal aorta is demonstrated. b, Second patient showing the tense pulsating mass in left flank which encroached on costal margin above and iliac crest below. This was 1 year after initial aortogram and wiring. c, Sketch of relations of aortic aneurysm in Case 2. d, Aortogram 1 year after initial study and wiring shows spreading of wire and enlargement of aneurysm. A soft tissue mass extending into the left pelvis represents clot in the aneurysm. g, Aortogram 1 month after operation shows tortuous aorta due to elongation with normal lumen.

placed a few millimeters from the edge of the cuff and another row over the edge (Fig. 2f). On release of the clamps after 37 minutes of aortic occlusion some bleeding occurred but it was easily controlled. Aneurysmal wall and blood clots in various stages of dissolution were removed from the retroperitoneal area. The specimen weighed 1,750 grams. The vertebral bodies, spinal nerves and, in one area, dura were exposed to blood in the aneurysmal lumen (Fig. 2f). Most of the sac was excised, but there was a thick segment along the left iliac vessels which was left rather than risk damage to these structures. The aneurysmal sac was sutured over the vertebral bodies, and the aorta was wrapped with omentum.

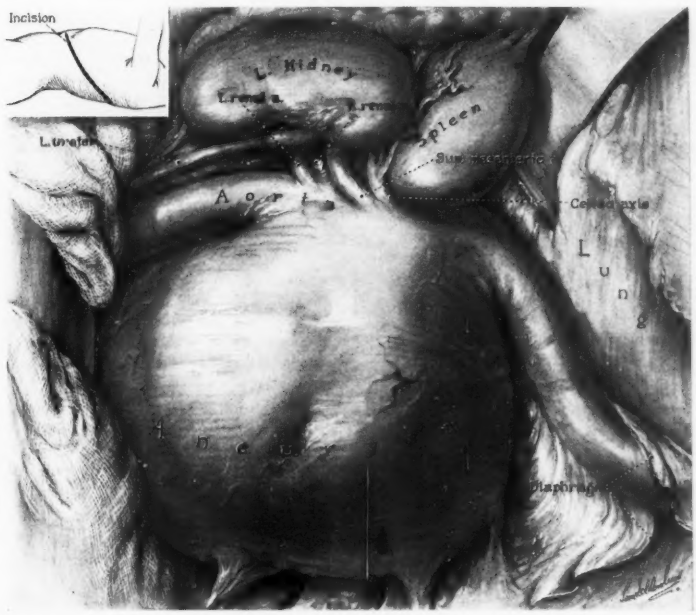


Fig. 2. e, Case 2. The large abdominal aneurysm displaced viscera and aorta forward and to the right. It extended into the pelvis and to elevate both leaves of the diaphragm.

After operation partial intestinal obstruction developed, and on the fourteenth day laparotomy revealed internal herniation through a defect in the mesosigmoid which had apparently been created at the original operation. Five days later an abscess in the left flank was drained. It apparently arose in the area where intestines had herniated through the mesosigmoid and where the segment of the aneurysmal sac had been left in the pelvis. The eroded vertebral bodies could be palpated but the aortic pulsation could not. Just prior to discharge a month after aneurysmectomy, aortography showed a tortuous but relatively normal aortic lumen (Fig. 2g).

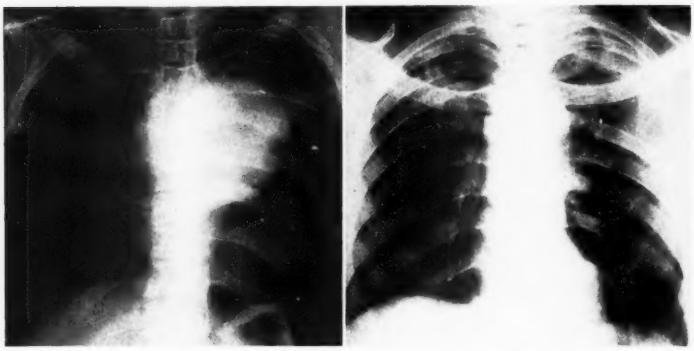
He was readmitted the following month because of bronchopneumonia. While in the hospital abscess pockets in the back and left flank were drained on several occasions. Ultimate saucerization of the left flank was required, which laid open the area where aneurysmal wall was left along the iliac vessels. This subsequently healed by granulation. Colonic and enteric fistulas developed and were closed surgically 8 months after excision of the aneurysm. He has been otherwise well.

Summary. This patient had a saccular aneurysm of the upper abdominal aorta which seemed to be well suited to wiring. In spite of 2 apparently satisfactory wiring procedures with an 8 month interval between them, the aneurysm contined to enlarge and excision was carried out. Although the aneurysm had attained large size, excision and restoration of the aorta were possible and the patient is alive and improved.

Case 3. W. McD., a 41 year old colored male, noted a sudden pain "under his heart" 2 years prior to admission while lifting heavy pipes. Nine months later his pains became worse and prevented sleeping. Cough and a weight loss of 50 pounds began. One year after onset he was admitted to the Johns Hopkins Hospital with recent appearance of venous distention over the left chest, neck, and arm, and exquisite tenderness and hyperesthesia over the sixth thoracic vertebra with fasciculation. He was never free from pain and required frequent narcotics.

Serological tests for syphilis were positive. Roentgenograms showed a posterior mediastinal mass with erosion of the fourth and sixth thoracic vertebrae. In April, 1951, an attempt at percutaneous wiring failed, and 2 days later a satisfactory insertion of wire was performed through an open thoracotomy. Nylon cloth, treated with a solution of radiographic film and previously found to be fibrogenic in the dog, was sutured about the aneurysm. He was symptomatically relieved and was discharged without sedatives. Pain returned in 4 months and attempted wiring was unsuccessful. Chordotomy was considered for his pain.

Eight months later he was readmitted because of a mass in the left middorsal area which his wife had



a b

Fig. 3. Case 3. A 41 year old man with intractable pain was temporarily relieved by electrothermic coagulation of the aneurysm. Extension of the aneurysm occurred 8 months later. At operation the aorta was occluded proximal and distal, the aneurysm of the thoracic aorta was removed, and the aorta reconstructed. His pain was relieved. a, Roentgenogram 1 year after initial wiring. The wire has spread and the mass enlarged. A tuberculous cavity was present in the right apex. b, Postoperative roentgenogram showing removal of aneurysm and some clearing of the tuberculous process.

noted over the preceding 8 weeks. An intermittent cough had developed. He was in obvious distress again and was anxious for relief of pain. A tender pulsating mass, 7 by 6 centimeters, was felt subcutaneously just to the left of the fifth to seventh thoracic vertebrae. Roentgenograms showed enlargement of the mass and spreading of the wire (Fig. 3a). There was infiltration in the left lower lobe and at the right apex with a cavity in the latter area. He had a low grade fever and acid fast bacilli in the sputum. The administration of streptomycin and para-aminosalicylic acid was begun. In the subsequent week the mass in his back became less pulsatile and the skin more edematous. Aspiration yielded sterile, brown material, and injected diodrast did not enter the aneurysm. On March 22, 1952, the aneurysm in the thoracic aorta, 2 inches distal to the origin of the left subclavian artery, was exposed through a posterolateral incision. The aneurysm was excised and the aorta reconstructed from aneurysmal wall, the aorta being occluded for 20 minutes. Closure by means of sutures was similar to that employed previously. Vertebral bodies and spinal nerves were exposed to blood and clot (Fig. 3c). The aneurysm communicated with the subcutaneous mass, but fresh clot occluded the opening. Except for the aneurysm the aorta appeared grossly normal. After operation he was completely relieved of pain. Seven months later he is continuing treatment for tuberculosis but is otherwise well.

Summary. This patient with a saccular aneurysm of the thoracic aorta obtained temporary relief from an apparently satisfactory wiring procedure under direct vision. A subcutaneous extension appeared and death was almost certain without further treatment. The aneurysm was excised and the aorta reconstructed during occlusion of the aorta for 20 minutes. Recovery was uneventful.

CASE 4. H. M., a 53 year old colored male, was referred to the tumor service of the U. S. Public Health Service Hospital in Baltimore because of a mediastinal mass. He was essentially asymptomatic. Dr. E. Converse Peirce, II, diagnosed an aortic aneurysm on fluoroscopy and confirmed the diagnosis by angiocardiography, in which the wall of the sac appeared thin and without clotting (Fig. 4a). There was no evidence of aortic insufficiency or other cardiovascular disease. He was given penicillin for latent syphilis. On April 17, 1952, with the assistance of Dr. Peirce, the aneurysm was well exposed through an anterior fourth interspace incision, the sternum being split in the midline. The aneurysm arose from the anterior surface of the ascending aorta and was located within the pericardial sac (Fig. 4c). The base of the aneurysm was occluded by two curved multitoothed Potts coarctation clamps. The sac was excised and the aorta sutured as in the previous cases. His recovery was uneventful and 6 months after operation he was asymptomatic.

Summary. A 53 year old man without symptoms was found to have a saccular aneurysm of the ascending aorta. Aortography demonstrated a thin wall without clotting. Excision of the sac and aortic suture were easily accomplished.

Aneurysms of the ascending aorta are frequently asymptomatic until of large size. The anterior surface of the ascending arch is in the most accessible region of the aorta. It is understandable that the first attempts at excision were for an aneurysm in this region. The aorta at this level obviously cannot be occluded so that one must be able to clamp the base of the sac in order to excise it.

CASE 5. R. D., a 56 year old white male, was referred by Dr. J. Earle Moore because of aneurysm of the aortic arch. Primary infection occurred in 1919 and inadequate treatment for syphilis had been given during the secondary stage. Over 1 year prior to entry he had pain in the chest and epigastrium. Five months later hoarseness appeared insidiously and examination showed paralysis of the left vocal cord. Dilatation of the aortic arch was seen on roentgenograms. Seven months after onset of symptoms pain became more severe and sharp with radiation to the back and down the left arm. He was treated with penicillin and had a complete remission of pain after 3 days of treatment. About a year after symptoms began he was admitted for evaluation for operation. There was a brassy nonproductive cough, a diastolic thrill in the third left interspace and a long aortic diastolic murmur. Angiocardiogram by Dr. R. Sloan showed obstruction of the left pulmonary artery and fusiform dilatation of the ascending aorta starting 1 centimeter or more above the aortic valve. There was a small saccular bulge on the anterior surface (fig. 5a). Another aneurysm was seen in the region of the junction between ascending aorta and the transverse arch. It was hoped this was a saccular aneurysm arising from the transverse arch. Under this impression and because of the extremely poor prognosis without treatment, a posterolateral thoracotomy was performed on May 3, 1952. A large aneurysm completely filled the concavity of the aortic arch. The left pulmonary artery was flattened against it (Fig. 5b). In attempting to free the posterior surface of the aneurysm, a finger was inserted into it and fatal hemorrhage occurred. Further examination showed a diffuse dilatation beginning just distal to the aortic valve and extending to the end of the aortic arch, beyond which the aorta appeared normal. A saccular component arose from the dilated arch opposite the origin of the great vessels. There was no clot anywhere in the aneurysm.

Summary. This patient was explored with a probably unjustified hope that a saccular aneurysm arose from a relatively normal aortic arch in spite of the fusiform dilation of the ascending aorta. Demonstration of the origin of aneurysms in this region is especially difficult by angiocardiography because of many superimposed shadows. The danger of dissection about a thin walled aneurysm is apparent and should be avoided whenever possible.

CASE 6. S. T., a 52 year old negress, noted a swelling in her neck in December, 1950. This increased progressively in size. A morning cough developed and she became hoarse and lost weight. There was occasional pain in the region of the mass. When first admitted in May, 1951, she had a blood pressure of 208/100. There was inspiratory stridor and a vigorously pulsating mass in the lower neck anteriorly. There were signs of aortic insufficiency. A roentgenogram showed a left superior mediastinal mass. Wiring was done percutaneously into the cervical mass with two 10 meter segments, only one

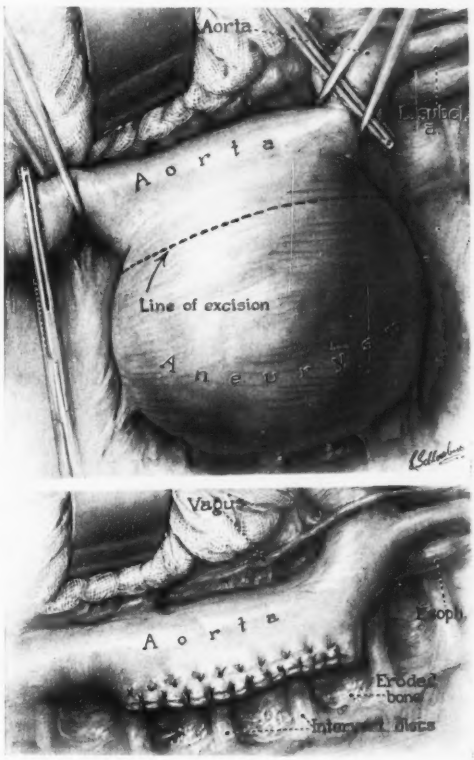
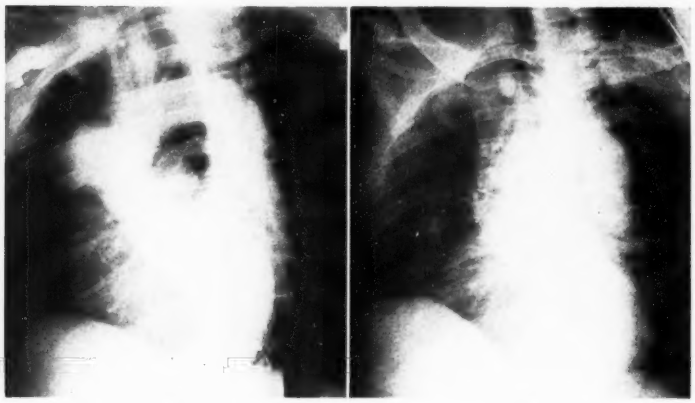


Fig. 3. c, Case 3. Drawings of aneurysm of the upper thoracic aorta and reconstruction after excision. Eroded vertebral bodies can be seen. These were in contact with the blood stream.

of which could be heated. Later roentgenograms showed that most of the wire was in the superior mediastinal mass (Fig. 6a). Her voice became less hoarse after wiring but there was no objective change in the size of the neck.

She was well for about a year and then returned because of increased dyspnea, dysphagia, and pain radiating through to her back. The mass seemed slightly larger (Fig. 6b). An aortogram showed a large aortic arch (Fig. 6d); the convexity of the arch could not be delineated. Injection into the aneurysm showed incomplete clotting. The diodrast was quickly washed through by flow of blood. On June 16, exploration was done through the left second interspace and the split sternum. The sternum was later divided through to the right second interspace. There was an innominate aneurysm involving the origin of the artery from the aorta and all of the vessel except its distalmost portion. The right common carotid and subclavian arteries were temporarily occluded, and a curved Gross coarctation clamp



a b

c

Fig. 4. Case 4. A 53 year old man with asymptomatic mediastinal mass. Angiocardiogram showed thin walled aneurysm of the ascending aorta. The base of the aneurysm was clamped and the sac excised. Recovery was uneventful. a, Aortogram by Dr. E. Converse Peirce showing saccular aneurysm of the ascending aorta. b, Postoperative aortogram after excision of aneurysm. c, Intrapericardial aneurysm of the ascending aorta. Multitoothed Potts clamps were applied from either end of the aneurysm and the aneurysm excised.

was applied to the convexity of the proximal arch of the aorta. The aneurysm was excised, and an 8 centimeter long opening in the aorta was sutured as described in other cases (Fig. 6e). An additional aneurysmal dilatation was present in the distal aortic arch. This was not disturbed since on angiocardiography it appeared to be fusiform with laminated clotting. Later posterolateral exploration may be necessary. She was completely relieved of pain, dyspnea, and dysphagia and was discharged in 2½ weeks (Fig. 6c). She was well when seen 4 months after operation.

Summary. A 52 year old negress was operated upon for an aortic-innominate aneurysm which caused marked dyspnea, dysphagia, and pain. The aneurysm had not been completely arrested by previous wiring. Although the saccular aneurysm had largely clotted, the presence of the mass caused considerable disability which could not be relieved without excision of the aneurysm. Blakemore (5) and Cooley and De Bakey have reported excision of somewhat similar aneurysms.

CASE 7. C. C., a 49 year old registered nurse, was well until she suffered severe injury to her chest in an automobile accident on October 1, 1950. Several ribs and the body of the first lumbar vertebra were fractured. After regaining consciousness she was dyspneic and had a sense of painful compression in

a

b

Fig. 5. Case 5. A patient with fusiform dilatation of the ending aorta had a saccular component in the concavity the aortic arch. It was mistakenly believed that the sacular aneurysm arose from distal, relatively normal aortic arch. The fusiform dilatation was inadvertently entered during operation with fatal result. a, Angiocardiogram showing fusiform dilatation of the ascending aorta with small saccular component on the anterior surface. The saccular aneurysm in the concavity of the arch was erroneously interpreted as arising from distal, relatively normal aorta. b, Operative exposure was made of fusiform and saccular dilatation of entire aortic arch. Excision was not possible.

e midsternal region. Hoarseness was noted by atives 48 hours after the injury. Roentgenograms ken soon after the accident showed no abnormality side the bony thorax.

On the tenth day of hospitalization following the accident she had one episode of tachycardia lasting out 4 hours, a feeble pulse, and hypotension which could not be explained by her physicians. Not during her 2 weeks' hospitalization could a blood pressure measurement be obtained in her left arm.

In the first month following discharge from the hospital progressive hoarseness appeared, and an intermittent, severe pain seemed to radiate from the interscapular to the midsternal region; this was associated with a choking sensation. Repeat roentgenological examination showed in the upper left mediastinum a pulsating mass which was at first interpreted as a hematoma. When the shadow did not decrease in size over several months a diagnosis of aneurysm was made and she was referred to Dr. H. William Scott at this hospital in June 1951. Slight hoarseness persisted but pain, discomfort, and dyspnea had largely disappeared.

Significant physical findings were a weak left radial pulse and a blood pressure measured as 90/80 millimeters of mercury in the left as compared with 135/80 millimeters of mercury in the right arm. Serological tests for syphilis were negative. Roentgenogram showed healed bilateral fractures of the third ribs and compression of the first lumbar vertebra. There was a mass in the upper left mediastinum which pulsated on fluoroscopy. Angiocardiography showed a saccular aneurysm at the terminal portion of the aortic arch. There was considerable clot in the wall.

In June, 1951, Dr. Scott performed a posterolateral thoracotomy and wrapped the lateral surface of the aneurysm with reactive cellophane which had been previously coated with dicetylphosphate and sterilized by soaking in aqueous zephiran. The entire surface of the aneurysm was not exposed. Convalescence was uneventful and she became asymptomatic. Her voice returned to normal about a month after operation, but hoarseness reappeared 4 months later.

In July, 1952, pain in the upper chest reappeared, at first only when the patient was tired but later more constantly. In September she returned for re-evaluation after Dr. Scott's departure from the staff. Roentgenograms showed slight enlargement of the shadow (Fig. 7a). Repeat angiocardiography showed no reduction in size or change in configuration of the aneurysm (Fig. 7b and c). Further operative treatment was thought to be indicated. On October 1, 1952, a left posterolateral thoracotomy was performed, re-entering the chest through the bed of the fifth rib. A short segment of the fourth rib was removed. The lung was mobilized, dissecting easily in the space surrounding the cellophane. Fibrous reaction was slight and not constricting. The aorta proximally and distally and the vessels arising from the arch were mobilized (Fig. 7d). The aneurysm appeared to arise from the terminal portion of the aortic arch. The left subclavian artery arose from the aneurysm itself. The medial portion of the aneurysm was thin walled and pulsating. The aortic arch just proximal to the origin of the left common carotid artery and the upper thoracic aorta were cross-clamped for 7 minutes, during which time the aneurysm was opened. A discrete circumferen-

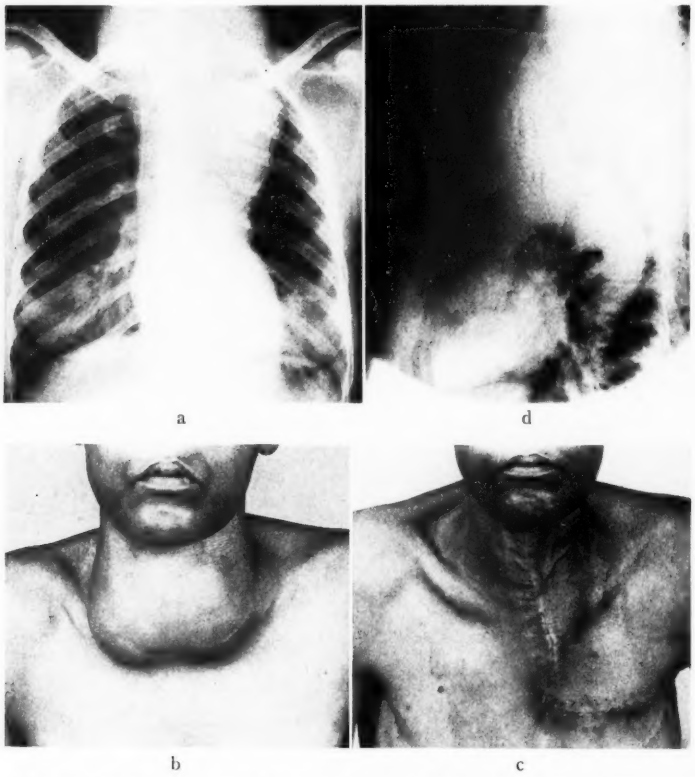


Fig. 6. Case 6. A 52 year old negress admitted because of an aortic-innominate aneurysm which caused marked dyspnea, dysphagia and pain. Incomplete clotting had been induced by wiring, but the presence of a mass made excision necessary for relief of symptoms. Relief was obtained. a, Preoperative roentgenogram of Case 6 showing upper left mediastinal and cervical masses. Most of the wire inserted percutaneously in the cervical mass had entered the mediastinum. b, Preoperative view of patient showing large pulsatile cervical aneurysm. c, Postoperative view after excision of aortic-innominate aneurysm. d, Angiocardiogram showing a dilated aortic arch. Position of wire indicated a thick concentric clot about the central, relatively regular lumen. Aneurysm of the distal arch did not fill with diodrast and was presumably largely clotted.

tial tear was seen in the aorta at the site of the origin of the left subclavian artery. The anterior portion of this was easily sutured from inside the aneurysm (Fig. 7e). Because of beginning hypotension and cardiac irregularity, cross-clamping of the aorta was discontinued before the entire opening could be sutured. The hole in the aneurysm was controlled by manual compression against the spine and aorta while the aneurysm was completely mobilized. Then Potts multitooth clamps were applied and the mouth of the aneurysm sutured as done in previous cases. Except for the mouth of the aneurysm, the aorta was grossly normal. Convalescence was uneventful and symptoms were relieved.

Summary. A 49 year old woman with a traumatic aneurysm of the distal aortic arch was initially treated by cellophane wrapping. Symptomatic relief was temporary and without objective change in the lesion. Excision of the aneurysm and preservation of aortic continuity was done with satisfactory early result. The essentially normal aorta, except for a localized rupture due to trauma, makes this type of aneurysm ideal for excision and aortic suture.

CASE 8. G. G., a 47 year old colored man, complained of dyspnea for 1 year and had noted a mass on his anterior chest 4 months before admission. He had occasionally noted a wheeze on expiration and for 3 months had experienced difficulty in swallowing

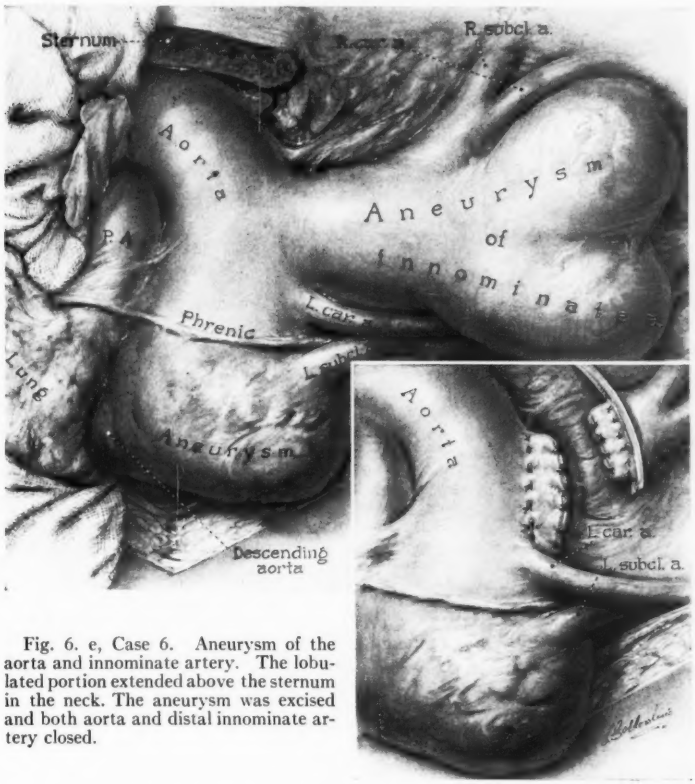


Fig. 6. e, Case 6. Aneurysm of the aorta and innominate artery. The lobulated portion extended above the sternum in the neck. The aneurysm was excised and both aorta and distal innominate artery closed.

with the sensation of food sticking behind his sternum. He began to sleep on his left side with one pillow and would waken at night whenever he rolled to the right side or back. He stated that in 1936 he was treated for about a year with weekly injections because of syphilis.

On examination he had a brassy cough and was unable to lie supine comfortably because of dyspnea. There was a 2 by 4 centimeter pulsating mass just to the right of the upper sternum. The pulsation could be stopped by pressure of one finger at the medial end of the first intercostal space. There were no signs of aortic insufficiency, and the heart was not enlarged. Roentgenogram showed a large mass in the right upper mediastinum (Fig. 8). On bronchoscopy the entire trachea was compressed in the anteroposterior direction, in some areas to approximately 2 millimeters. Angiocardiography demonstrated compression and partial obstruction of the superior vena cava. There was less diodrast seen in the left lung than the right, suggesting obstruction to the left pulmonary artery. The aortic arch was not clearly visualized but appeared dilated. Injection directly into the aneurysm showed that most of the mass consisted of clot, although there was a central area which filled with diodrast.

Stainless steel wire was inserted on October 6, 1952 to promote clotting and to gain information concerning the configuration of the aneurysm. Later roentgenogram showed loops of wire in a dilated aortic arch which was displaced to the left and posteriorly. It was believed that the widened mediastinum and obstruction to the left pulmonary artery were caused by displacement of the aortic arch by a large saccular aneurysm. At thoracotomy on October 15, 1952 this proved to be correct. Incision was through both third intercostal spaces and across the sternum. A large saccular aneurysm arose from the anterior surface of the ascending aorta just proximal to the innominate artery. Marked respiratory obstruction was relieved by retraction of the sternum. The neck of the aneurysm could be surrounded, but it could not be separated from the innominate artery. A linen-shod intestinal clamp was placed across the convexity of the aortic arch in this region with the plan of reconstructing the innominate artery if possible. There was considerable bleeding when the aneurysm was opened until

a b c

Fig. 7. Case 7. A 49 year old woman with traumatic aneurysm of the distal aortic arch was initially treated by cellophane wrapping. Symptomatic relief was temporary and without objective change in the lesion. Excision of the aneurysm and preservation of aortic continuity was done with satisfactory result. a, Roentgenogram showing upper mediastinal mass 15 months after wrapping with cellophane. There had been no reduction in size of the lesion. b, c. Anteroposterior and lateral angiocardiograms showing a saccular aneurysm of the distal aortic arch. Considerable clot was present in the lateral portion. Essentially similar findings were obtained 15 months previously.

the distal innominate artery was occluded by pressure against the aneurysm. During closure of the mouth it became apparent that the clamp occluded both innominate and carotid arteries. The lumina of these arteries were reconstructed and the aorta successfully sutured, but both vessels had been occluded for about 35 minutes, during which time the arterial pressure was low because of blood loss.

The patient never recovered consciousness and died 17 hours after completion of the operation. Autopsy showed a satisfactory closure of the aorta. Loops of stainless steel wire with some enmeshed clot extended across the orifices of the innominate and carotid arteries. Death was ascribed to cerebral ischemia during the operation.

Summary. A patient with dyspnea and dysphagia caused by a large saccular aneurysm of the ascending aorta was treated by excision of the aneurysm, suture of the aorta, and reconstruction of the innominate artery. In retrospect, introduction of the wire into the aneurysm was disadvantageous, since it and enmeshed clot partially obstructed the great vessels. The size of the aneurysm prevented good exposure of the great vessels arising from the aortic arch, and during excision of the aneurysm the left common carotid artery was inadvertently occluded along with occlusion of the innominate artery. The patient never regained consciousness.

DISCUSSION

Aneurysm of the aorta is usually caused by arteriosclerosis or by syphilis. On the basis of the type of aneurysm, its location in the aorta, age of the patient at onset, and the symptoms and signs, the specific cause can be determined clinically with reasonable certainty. The uncommon aortic aneurysms due to trauma and infection in most respects resemble those due to syphilis. The relative incidence of the two common types of aneurysm corresponds rather closely to the prevalence of venereal disease. Thus Kampmeier (19, 20) in reports from New Orleans writes almost entirely of thoracic and upper abdominal aneurysms due to syphilis, whereas Estes at the Mayo Clinic attributed only 2 of 102 abdominal aortic aneurysms to causes other than arteriosclerosis.

As Scott reported from this hospital, arteriosclerotic aneurysm of the aorta almost invariably occurs in the terminal aorta, below the origin of the renal arteries. The disease is more common in males and, as with other manifestations of arteriosclerosis, occurs in the older age groups. The average age of Estes' 102 patients with abdominal aneurysm was 65 years. Pain and an abdominal mass are the most frequently noted symptoms, but about a third of the patients are free of symptoms. The pain is usually poorly localized, ill defined, referred to both front and back, and

nonradiating. The majority of arteriosclerotic aneurysms of the aorta are fusiform. In general they do not produce erosion of the vertebral bodies; erosion was seen in only 7.5 per cent of Estes' patients in whom roentgenological examination was done. It seems that arteriosclerotic aneurysms usually result from concentric dilatation, elongation, and thinning of the entire circumference of the vessel. Elongation pushes the vessel forward and away from the vertebral bodies and nerve roots, and in the absence of localized rupture of saccular aneurysm there is no vertebral erosion or root pain. Calcification is commonly seen in the wall of the dilatation on roentgenography.

The prognosis for the patient with this type of lesion without operation is probably better than for patients with syphilitic aneurysm. Estes compared survival rates of patients with abdominal aneurysm and normal patients of the same age group. Whereas 65 per cent of the normal population aged 65 survive 5 years, only 67 per cent of the patients with abdominal aneurysm survived 1 year; 10 per cent survived 8 years. None of the 8 patients who could be followed lived for 10 years. Sixty-three per cent of the patients died from rupture of the aneurysm.

Syphilitic aneurysm of the abdominal aorta, on the other hand, is usually located at or above the origin of the renal arteries and only rarely appears below this level. It is seen in younger individuals. Six of Kampmeier's (19) patients were between 20 and 25 years, 67 per cent under 45 years, and only 8 of the 73 were above 55 years of age. Pain was present in 92 per cent of the patients and tenderness on palpation in many. Seventy-five per cent of the patients who had films of the spine showed vertebral erosion with preservation of the intervertebral discs. There was evidence of vertebral erosion in 10 patients, accompanied by radiation of pain, which was undoubtedly due to irritation of the nerve roots. The prognosis is considerably poorer than with an arteriosclerotic aneurysm, as most of Kampmeier's patients died within 6 months from onset of symptoms, the majority from rupture.

Syphilitic aneurysm occurs 5 to 10 times more frequently in the thoracic than in the abdominal aorta. Occasional aneurysms in the thorax may be caused by trauma or infection other than syphilis, but almost never by arteriosclerosis in the absence of other disease. In Boyd's 4,000 reported cases, aneurysms occurred in the ascending, transverse, descending arch and thoracic aorta in the ratio of 10, 7, 3, 1 respectively. Because of the clinical picture, which probably depends upon anatomical relations, those of the ascending arch have for years been called aneurysms of signs, those of the transverse arch, aneurysms of symptoms. In order of frequency pain (65 per cent), dyspnea (60 per cent), and cough (54 per cent) were the commonest symptoms in Kampmeier's large series (20). Aneurysms of the transverse and descending arch often cause hoarseness and dysphagia. Pain was

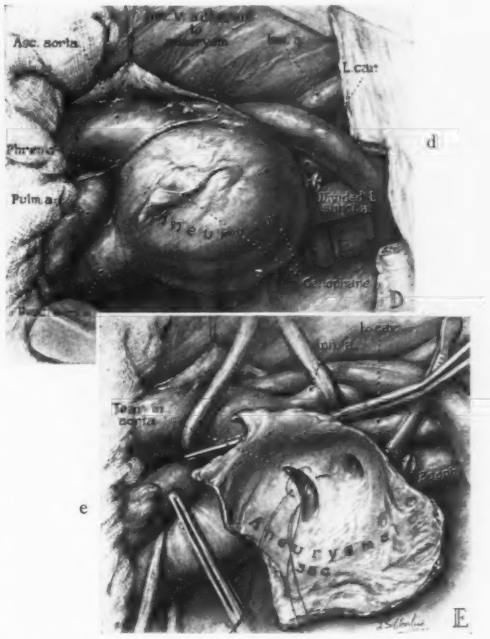


Fig. 7. d, e, Case 7. Posterolateral exposure of aortic arch and mediastinum. The aneurysm arose from the distal portion of the aortic arch, probably at the site of origin of the left subclavian artery since this vessel arose from the aneurysm. A thin layer of fibrous tissue enclosed the previously applied reactive cellophane. The aneurysm was opened and excised after the aorta was clamped proximally and distally. The circumferential tear in the aorta was sutured and adjacent aneurysm sac sutured over the defect.

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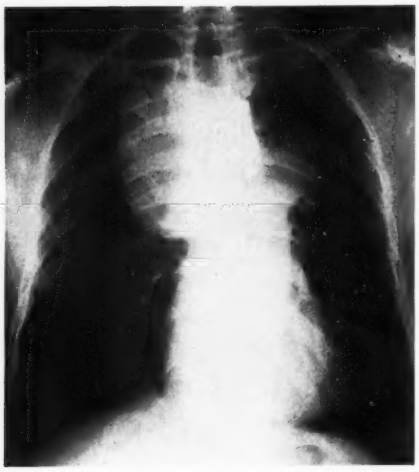

Fig. 8. Case 8. Roentgenogram of a patient with dyspnea and dysphagia caused by a large saccular aneurysm of the ascending aorta which was treated by excision of the aneurysm, suture of the aorta and reconstruction of the innominate artery. During excision the left common carotid artery was inadvertently occluded along with occlusion of the innominate artery. The patient never regained consciousness.

present in 86 per cent of Kampmeier's patients with aneurysm of the thoracic aorta, probably because of proximity to posterior parietal nerves. On the basis of gross pathological anatomy seen at operation in the cases described in this report, it appears that severe pain due to aneurysm is often caused by localized rupture with formation of a false aneurysm and exposure of spinal nerves to the pulsating wall, or to the actual blood stream, as in Case 2. Padget and Moore have remarked upon pain in the chest as a symptom of syphilitic aortitis even in the absence of aneurysm. They attributed this pain to stimulation of nerve endings in the aorta itself.

The prognosis in patients with thoracic aneurysm is poor in respect to life; only 18 of Kampmeier's (20) 188 patients lived longer than 2 years after onset of symptoms, the average duration ranging from 6 to 9 months according to the location in the various regions of the intrathoracic aorta. Even the brief duration of life is often uncomfortable because of pain and respiratory or esophageal obstruction.

Syphilitic aortitis begins early in the course of acquired syphilis when, during the spirochetemia, the aortic wall is invaded by the Treponema pallidum. The lymphatics and vasa vasorum of the media are most severely affected, and an obliterating endarteritis, necrosis, and fragmentation of elastic tissue of the media occur. At autopsy 70 to 90 per cent of patients with late syphilis have evidence of disease in the aorta, but only a fraction of these will have symptoms of syphilitic cardiovascular disease. Of over 6,000 patients with late syphilis reported by Moore, Danglade, and Reisinger, 10.1 per cent had clinical cardiovascular syphilis, 2.7 per cent had aortic regurgitation, 1.2 per cent had aneurysms, and the others had aortitis, angina pectoris, myocarditis, and other cardiovascular lesions. If a diffuse weakening of the aortic wall occurs, fusiform dilatation results. On the other hand, there frequently is a localized area of weakness and rupture causing a saccular aneurysm of varying size but with a relatively narrow mouth. The duration of the disease from chancre to onset of complications of aortitis was 10 to 20 years in the majority of cases when determinable in Kampmeier's series (20).

Adequate arsenical and heavy metal treatment was effective in preventing the development of cardiovascular syphilis. There is every reason to believe that penicillin will be just as efficacious as arsphenamine, and to hope that syphilitic aneurysms will in time become rarities. However, there will continue to be patients in whom the diagnosis is not made or who are inadequately treated before the development of the complications of aortitis. Even in such instances benefit might be expected from antibiotic therapy. Moore and associates (28) showed that of 22 patients with aneurysm who received little or no treatment 20 were dead with an average duration of life from onset of symptoms to death of 19 months. With adequate treatment the mortality at that time was 40 per cent with an average duration of 75 months from onset of symptoms to death. Hu, Liu, Chen, and Frazier were able to recover viable Treponema pallidum from the aorta in a patient with aortitis, indicating continuing activity presumably amenable to treatment.

Although syphilitic aneurysm is a complication of a more generalized aortitis, it is usually the most dangerous aspect of such disease and, after adequate penicillin therapy, may be the only lesion threatening the patient's life and well-being. The aorta elsewhere and immediately adjacent to the mouth of a syphilitic aneurysm may be only slightly diseased. The poor prognosis without treatment and the relative normality of other parts of the cardiovascular system are a stimulus to attempts at direct treatment of aneurysm.

Aneurysm of the aorta may be caused by a severe blow to the thoracic cage or, less commonly, to the abdomen. Such an aneurysm results when the layers of the aortic wall are incompletely torn by blunt trauma or fractured bony parts. More frequently there is a complete laceration and rapid death. The tear is usually circumferential and, even when only the intima is torn, clean cut. The sites of predilection are in the ascending arch, just distal to the aortic valve, and in the region of the duct of Botalli and left subclavian artery. Prior to the frequent use of reliable serological tests for syphilis, many aneurysms were attributed to trauma which were probably caused by Treponema pallidum. Traumatic aneurysms, even more than those due to syphilis, invite a direct attack because of the localized lesion.

Numerous methods have been used in the treatment of aneurysm of the aorta with less catastrophic results than the first attempt at cure of Valisnari's patient, mentioned earlier. Aneurysms often undergo spontaneous clotting of varying but unpredictable degree. Complete clotting is responsible for the occasional case of "Nature's cure." After clotting occurs in a fusiform dilatation one is left with a vessel of large external diameter but possibly normal internal diameter and a thick wall of clot. After solid clotting in a saccular aneurysm the tumor may in time contract. According to Laplace's law the tension required in the wall of a vessel to prevent disruption varies with the diameter of the structure. Hence solid clotting reduces the diameter and the tendency to rupture, but in either type of aneurysm dissection may subsequently occur beneath the clot, with greater dilatation or rupture. Many of the methods of treatment now solely of historical interest, such as acupuncture, galvanopuncture, and the injection of gelatin, were aimed at the production of mass clotting. Surgical treatment which has been of more than passing interest may be grouped under the following headings: ligation, introduction of wire into the aneurysm, use of fibrogenic or reinforcing materials about the aneurysm, endo-aneurysmorraphy, and resection.

Ligation of the aorta for aneurysm has been used primarily for an involvement of the lower abdominal aorta; usually the ligature is placed just proximal to the dilatation, a principle first enunciated by Anel in 1710 (25) and at present often applied with success to aneurysms of peripheral vessels. When applied to the aorta, results have been less successful. Forty-five attempts to occlude the aorta by ligation were recorded prior to 1951 (12). None of the 21 recorded instances before 1918 resulted in a cure. Since that time half of the patients so treated survived 6 months and several over a year. The need for gradual occlusion of the aorta while collateral vessels develop and the heart adjusts to the increased resistance to flow has been recognized, and attempts have been made to meet this need by methods including Halsted's aluminum bands, elastic ligatures, repeated operations with progressively tighter constriction, and the use of fibrogenic substances. Ligation of the aorta obviously offers little likelihood of survival unless performed distal to the major abdominal branches; hence this method is applicable primarily to arteriosclerotic aneurysms.

Ligation of the main trunk distal to an aneurysm (Brasdor 1798) or of one or two of its main branches (Wardrop 1825) (25) has been attempted infrequently and without notable success. Guinard advocated this principle for aneurysms of the great vessels at the base of the neck. He argued that the origin of most of these aneurysms could not be determined clinically, and he employed distal ligation of the right common carotid and subclavian arteries for all. Although this is technically a relatively simple operation, ligation of the aorta above the renal arteries has been invariably fatal, and it is unlikely

that ligation of the great vessels arising from the aortic arch will arrest aneurysm of the aorta itself.

Wire was first introduced into an aneurysm by Moore in 1864 (27). Since then, variations of this method have included the use of fine metal watch springs, wire wisps, great lengths of fine stainless steel, and various means of heating or electrolysis. Borrie and Griffin report arrest of aneurysm for periods of 12 to 32 months in 5 of 9 patients treated with Colt expanding wire wisps. These were all saccular aneurysms due to syphilis. Two of the remaining 4 patients died of tracheal compression for which the operation was performed, one from aortic obstruction when a clot caught on one of the wire meshes, and one from heart failure 16 months after successful wiring. Only 2 of 13 patients who refused or were unsuitable for such treatment survived even their 9 months' period of observation. The greatest refinement of this method has been achieved by Blakemore and King (7) by using fine insulated coin silver wire which can be heated. Such fine wire attains a temperature which induces clotting only in those areas of the vascular channel where flow is not so rapid, thus producing a selective concentric clotting and reinforcing the periphery or saccular components of aneurysms. Blakemore (5) reported a 10 year follow-up on patients with saccular aneurysms treated by his technique. Twenty-seven per cent were living, almost all working and essentially symptom free. Unfortunately, the wire used requires special insulation and is not now available.

Using the special wire given to Dr. Blalock by Dr. Blakemore and Blakemore's technique as modified by Owings, various Hopkins staff members have employed this method. Some excellent results with complete arrest of activity have been obtained; however, reactivation such as occurred in Cases 1, 2, and 6 has been common in our experience. Blakemore (6) obtains some impedance and turbulence of blood in the aneurysm by application of an elastic ligature over reactive cellophane proximally and inserts fine wire directly into the tumor. This treatment aims at slow occlusion of the terminal aorta, an acceptable but not ideal end result.

Endo-aneurysmorraphy as described by Matas is an excellent and established procedure for treatment of aneurysms of peripheral arteries. By occluding the parent vessel and opening directly into the sac, one of three methods may be used. Where the vessel can be sacrificed, the sac may be obliterated from the inside, preserving, as in all applications of this method, the collateral vessels which may be intimately associated with the wall of the sac. In case of a saccular aneurysm one may be able to suture the neck of the sac and thus perform a restorative endo-aneurysmorraphy. Matas originally proposed a reconstructive type for fusiform aneurysms, but it was learned that the reconstructed arterial segment soon thrombosed, and this procedure was abandoned except in special instances. Matas made a point of preserving aneurysmal wall and the collaterals in it but obliterated the dead space of the sac by suture. For obvious reasons endo-aneurysmorraphy has rarely been applied to the aorta. In only the last of 5 reported instances did the patient survive (4). Woods and Kenney have described successful obliteration of a congenital aneurysm of the descending aorta. Plication and aneurysmorraphy were performed without opening the sac.

The use of fibrogenic and reinforcing materials has gained great popularity in recent years based upon Page's original use of cellophane about the kidney to produce hypertension. Pearse demonstrated variable response when it was applied to the great vessels in the dog, and Harrison and Chandy reported the first clinical use in attempting constriction of the great vessels in man. Poppe and Renault de Oliveira clarified the variable response obtained by demonstrating differences in various types of cellophane, and Yeager and Cowley identified the fibrogenic property as due to dicetylphosphate. Recently, numerous workers in the Surgical Hunterian Laboratory at this institution have attempted to constrict large vessels in the dog by the use of various fibrogenic substances. Although a great deal of fibrosis can be produced, we have not been impressed with subsequent constriction of arteries. Theoretically one might expect the pulsating intravascular pressure to dilate

a scar rather than to allow it to contract. Partial constriction at the time of the initial application or induction of inflammation in the vessel wall may lead to subsequent clotting and possibly accounts for the occasional arrest and cure. Abbott applied cellophane to 32 patients with thoracic aneurysm. Follow-up studies were not complete, but he did not believe life was prolonged in any of the patients with advanced disease. The only benefit claimed was relief of pain in 40 per cent of the cases. The difficulty of surrounding saccular aneurysms which have eroded bone or other important structures was remarked upon. An aneurysm is only as strong as its weakest area, and frequently this area is the one where dissection cannot be free enough to permit wrapping with cellophane. This method seems more applicable in cases of fusiform aneurysm. In such instances the material may simply reinforce the wall rather than produce constriction as a result of scar contraction. Lowenberg used cutis grafts and Grindlay and Waugh a nonreacting polythene sponge for this purpose. That cellophane may not perform the function ascribed to it is suggested by Aird's report of a patient who obtained a good result following banding of an aneurysm but passed part of the cellophane per rectum a year later.

Excision of an aortic aneurysm is often feasible because of two features of pathologic anatomy which are not generally recognized. In the first place the rupture in the aorta, or the mouth of the aneurysm, is usually of small diameter compared to the size of the aneurysm itself. This fact has been cited as an argument for the use of other methods of treatment. In the first patient in whom Moore inserted wire in 1864, the mouth of the aneurysm of the ascending arch was found to be no larger than a sixpence. Secondly, although the aorta adjacent to the aneurysm and elsewhere may show signs of disease, it is often functionally adequate, and with penicillin therapy there is at least hope of arrest of the inflammatory process and of prevention of disturbance of function. The enlargement of saccular aneurysms so frequently noted is due more to rupture of the aneurysm itself than to extension of the aortic opening. Tissue at the mouth of the aneurysm is usually fragmented aorta and tough scar tissue which are fully capable of holding sutures. This is less true in the case of fusiform aneurysm where an occluding clamp may tear the aorta.

Tuffier (40) had a good idea of the pathologic anatomy of aortic aneurysm when he planned the first excision in 1902. When presented with a woman with an aneurysm of the ascending aorta he procured 8 specimens from the Musée Dupuytren in each of which excision was feasible. He planned an excision on the basis of this study. At operation he was able to expose the narrow neck of the sac but, gratified at having progressed so far without undue difficulty, he abandoned his initial plan to excise the sac and simply ligated the neck. The sac became gangrenous, presumably infected, and the patient died from hemorrhage 13 days later. Tuffier was roundly abused in the medical society for attempting such a procedure and did not attempt it again until 1909 (41). On this occasion he inadvertently entered the aneurysmal sac, quickly thrust his finger into the neck of the sac to tamponade it, and then sutured a "sterilized, American glove, extremely supple and very thin which [Tuffier] almost exclusively was using in surgery [in France] at that time," to the orifice over his finger and left the rubber tissue as a stopper. The rubber tissue was replaced after drainage appeared on the fifteenth day, but the patient died 2 days later, presumably of hemorrhage. Kümmell refers to an additional case with fatal outcome which Tuffier attempted, but the original report cannot be found. Tuffier stated that for aneurysms of the aortic arch to be amenable to surgery they should be "accessible, isolable, and extricable." Advances in surgery have made each of these conditions more readily met.

Reports of successful excision of aortic aneurysm are few in number, excluding those in conjunction with coarctation of the aorta, referred to later. Meyer, Monod, and associates demonstrated during thoracoscopy a pulsating mass which bled when punctured, and Monod performed exploratory thoracotomy and excised an aneurysm from the thoracic aorta by clamping and suturing the neck. The presence of congenital anomalies of the aortic

arch and the histology of the specimen led them to believe that the aneurysm was congenital in origin. They believed syphilitic aneurysms could not be removed and that such aneurysms were not surgical problems. Ochsner inadvertently entered an aortic aneurysm during exploration for a mediastinal mass. It was excised and the mouth sutured. Blakemore in 1947 (4) and Cooley and De Bakey in 1952 reported excision of aneurysms of the innominate artery involving the aorta which were treated by clamping and suturing the aorta at the base of the innominate as suggested and done on a cadaver by Rundle in 1937 and as performed in Case 6 reported here. Lam and Aram reported replacement of the thoracic aorta by homograft for aneurysm. In this patient as well as in Tuffier's first and in 1 reported by De Bakey and Cooley, failure to resect the aneurysm led to later difficulty and death, although the patient of Lam and Aram lived 3 months. Cooley and De Bakey report an additional patient in whom they excised a saccular aneurysm of the ascending aorta. He died 14 hours after operation of cerebral complications attributed to anesthesia. In the terminal aorta DuBost and associates excised a fusiform arteriosclerotic aneurysm and substituted a homograft from the same region. Wylie, Kerr, and Davies excised a segment from the anterior wall of a fusiform aneurysm, and a similar unreported procedure has been performed by the author.

Beginning with the report of Alexander and Byron in 1944, several authors have reported excision of aortic aneurysms in connection with treatment of coarctation of the aorta, and several such patients have been treated by Blalock and his staff at this hospital. As remarked by Shumacker, the presense of coarctation makes occlusion of the aorta less dangerous and a different problem from aneurysms elsewhere when coarctation is absent.

Except for Tuffier and more recently Cooley and De Bakey, even those authors who have reported excision of aortic aneurysms have not advocated this as the method of choice for syphilitic saccular aneurysms. In fact, some have gone so far as to state that success with this treatment would not be likely. The cases described in this report indicate that saccular aneurysms in any area of the aorta can be excised. In the area proximal to the origin of the left common carotid artery one must be able to clamp the neck of the aneurysm since the aorta itself cannot be occluded, and in this region one must be able to preserve at least one common carotid artery. It may be feasible in some instances to anastomose an innominate or a carotid artery to the reconstructed aorta, but the thickened fibrous tissue about the aneurysm is more suited to simple closure than to plastic repair. Distal to the origin of the left subclavian artery one can clamp the aorta for a brief period while the aneurysm is excised and a lumen reconstructed. Hence even fusiform aneurysms arising in the thoracic aorta or lower are amenable to this type of treatment. It is possible that the use of temporary shunts may allow the replacement of segments of the aortic arch, but this has not yet been accomplished in a patient.

Brief consideration might be given to some of the principles which at present are second nature to one interested in cardiovascular surgery but which required more conscious thought a few years ago. Tuffier enunciated the sound principle of avoiding mobilization of the peripheral areas of the aneurysm, particularly when bone erosion is present, until the neck of the aneurysm has been controlled. When the aorta is to be occluded, dissection and control of this structure must be attained before the aneurysm is attacked. Numerous instruments have been described to occlude vessels. The curved and straight modified intestinal clamps as described by Gross and the multitoothed Potts clamps have been best fitted to the work described here. It is important that clamps not be placed on the aneurysmal wall, particularly of a fusiform dilatation. The attenuated wall tears easily and repair is extremely difficult. This thinning of the wall probably precludes excision of fusiform aneurysms located proximal to the distal portion of the aortic arch. The wall of a fusiform aneurysm may be approximated by multiple sutures where a clamp will cut through.

Multiple interrupted sutures have been employed. A row of mattress No. 0000 silk sutures several millimeters back and an additional row over the cut edge have worked

satisfactorily. In 1 instance sutures were placed proximal to the clamp, in which case finger pressure to approximate the aortic walls prevented tearing of the aorta on tying the sutures. Tissue in the aorta and adjacent sac has always been too tough to allow use of the fine curved needles ordinarily employed for vascular suture. For this purpose Halsted's fine intestinal needles, resharpened after about one third of their length has been broken off, have been used.

The fatal results in patients of Tuffier, Cooley and De Bakey, and Lam and Aram and the infection in Case 2 reported here are sufficient evidence that the sac and contents must be removed to prevent later infection and possible rupture. Exposure must be liberal. When the anesthetist has proper control of respiration one need have little fear of splitting the sternum or of entering the opposite pleural cavity. The routine use of transfusions and antibiotics needs no comment. Similarly angiocardiography or aortography to visualize the aneurysm should be tried.

One patient seen by the author, in whom excision was planned, died of anoxia following bronchoscopy. Patients who are dyspneic because of aneurysm of the aortic arch are characteristically least dyspneic when leaning forward. Hyperextension required for bronchoscopy, as in the patient mentioned, may close off the trachea and at the same time increase the demand for oxygen because of excitement. When dyspnea is extreme, evaluation of the tracheal and bronchial compression should be done by laminagraphy. An endotracheal tube should be inserted past the obstruction under local anesthesia prior to operation.

SUMMARY AND CONCLUSIONS

Aneurysm of the aorta remains a major surgical problem in spite of many and varied forms of treatment previously advocated. Surgical treatment which has been of more than passing interest may be grouped under the following headings: ligation, wiring, use of fibrogenic or reinforcing materials about the aneurysm, endo-aneurysmorraphy, and excision. Consideration has been given to the historical aspects and advantages and disadvantages of each of these.

Saccular aortic aneurysms are usually caused by syphilis. They occur in middle aged patients and arise above the origin of the renal arteries. The aneurysm may be the only lesion threatening the patient's life and well-being. Frequently the opening into the aorta is small compared to the diameter of the aneurysm. Trauma or infection other than syphilis is responsible for an occasional aneurysm which, except for the absence of diffuse aortitis, clinically resembles those caused by syphilis. Arteriosclerosis characteristically caused a fusiform dilatation of the terminal aorta below the origin of the renal arteries. It is primarily a disease of elderly patients and is not as much a focal lesion as is syphilitic aneurysm.

The poor prognosis for patients with saccular aneurysm and the focal nature of this complication of aortitis or trauma stimulate attempts at a direct attack upon the aneurysm. Previous methods leave much to be desired.

Eight patients are reported with saccular aneurysms in different regions of the aorta. In 6, excision of the sac and suture of the aorta have been successfully carried out. The surgical technique has been discussed.

Resection of saccular aneurysm with preservation of aortic continuity is feasible in all regions of the aorta. It is the procedure of choice in many instances.

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AN EVALUATION OF THE EOSINOPHIL COUNT IN PATIENTS UNDERGOING MAJOR SURGERY

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IT has been demonstrated by Laragh and Almy and Roche and his associates that the eosinophil count falls to low values, frequently zero, in the early postoperative period within 4 to 8 hours after the incision in major surgical patients. Gabrilove showed a profound first day postoperative fall in eosinophils in patients undergoing gynecological surgery, such as vaginal repairs. Field and his associate have also demonstrated a greater than 50 per cent fall from the preoperative level when evaluating the second day postoperative eosinophil count. Roche and associates have shown from their study that the postoperative fall is usually maintained until the third day when the eosinophils have been noted to rise; and they concluded that postoperative eosinophil findings were related to changes in adrenocorticoid function, the fall in eosinophils being due to increasing 11–17 oxyglucocorticoid activity and the rise to a relative decreasing 11–17 oxyglucocorticoid activity.

The level of circulating eosinophils has been shown to fall in response, specifically, to the exogenous administration or endogenous production of 11–17 oxyglucocorticoids (compounds E and F), as occurs with the administration of compound E, compound F, ACTH, and nonspecific pituitary-adrenal stimulants such as epinephrine, ephedrine, insulin, and histamine. Compounds such as mineralocorticoids and other steroids have been shown to produce no fall, or insignificant falls, in the level of circulating eosinophils. These findings, as well as the increased urinary 11-oxysteroid excretion in the postoperative period, had been the basis for utilizing the *changes* in the eosinophil level after surgery as an index of adrenocortical function. Subsequently more direct quantitative correlations between eosinophils and 11–17 oxyglucocorticoids have been demonstrated, suggesting the significance of the *absolute* eosinophil level. Muehrcke and co-workers have shown that the eosinophil count falls significantly in vitro by incubating defibrinated blood with cortisone, but the count does not fall when incubating the defibrinated blood with antihistaminics. In addition to this in vitro direct relationship of decreased eosinophil counts with the presence of increased amounts of 11–17 oxyglucocorticoids, it has been demonstrated (10) that under certain conditions the absolute level of eosinophils in an individual is inversely proportional to the level of adrenocorticoid function in that individual as expressed by the urinary corticoid assays. Although the previous studies have emphasized the changes in the eosinophil count, rather than the absolute level of eosinophils, the object of this paper is to demonstrate that both indices, that is, the *absolute count* and the *per cent change* provide a practical means of evaluating adrenocortical function in the surgical patient, and also to present useful criteria for values of these indices.

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METHODS AND MATERIALS

Eosinophil counts were done in the clinical pathology laboratory by technicians during the daily hospital work routine. The method of Randolph was used in which the number of cells actually counted in the counting chamber was multiplied by the factor 11 to give the calculated number of cells per cubic millimeter of blood. Preoperative counts were done on 50 patients on the day of admission to the hospital, the day before surgery, between 3:00 and 6:00 p.m. The patients undergoing abdominal or pelvic surgery received spinal anesthesia alone or supplemented by inhalation anesthesia, while others had intravenous sodium pentothal. A tabulation of the types of sur-

TABLE I.—COMPILATION OF MAJOR SURGICAL PATIENTS STUDIED

Diagnosis	Type of surgery	No. of patients
Duodenal ulcer	Subtotal gastrectomy	12
Carcinoma of colon	Resection colon	8
Myoma of uterus	Total hysterectomy	6
Cholelithiasis, cholecystitis	Cholecystectomy	5
Carcinoma of stomach	Total gastrectomy	3
Teratoma, ovary	Oophorectomy with total hysterectomy	2
Diverticulitis: terminal ileitis; carcinoma, ileum; bowel obstruction with adhesions; colostomy; appendicitis; carcinoma, pancreas; medical jaundice	Resection, colon; right hemicolectomy; resection, small bowel; release of obstruction; closure of colostomy; appendectomy; cholecystojejunostomy; laparotomy with liver biopsy, respectively	8 (1 each)
Nodular thyroid; prolapse uterus; ganglioneuroma, duodenum; healed peptic ulcer; malignant tumor of groin	Thyroidectomy; vaginal hysterectomy; resuspension of uterus; excision of duodenal tumor; release of gastroenterostomy; removal of groin tumor with radical node dissection	6 (1 each)
	Total	50

gery and the principal diagnoses appear in Table I. All surgery was initiated in the morning hours usually at 7:00 or 9:00 a.m. Postoperative counts were done for all 50 patients on the first postoperative day at about 8:00 a.m. which was about 20 to 26 hours after the surgical incision. Morning counts were also done on the second and third postoperative days in 48 and 16 of the patients respectively. The absolute level of circulating eosinophils was recorded as the calculated number of eosinophils per cubic millimeter of blood. The per cent change was taken to be the comparison of the preoperative count with the count on the first postoperative day. Variations from 0 to 55 per cubic millimeter, since only 5 or less cells were actually counted, are allowable within the limits of inherent error introduced by Poisson's law of random distribution inherent in the counting chamber as described by Berkson. Therefore, initial counts of less than 60 per cubic millimeter cannot reveal a statistically significant change.

DATA AND RESULTS

Eosinophil counts preoperatively ranged from 0 to 803 in the 50 patients studied. The data obtained for the first postoperative day were evaluated by using two criteria for judging the "normal" eosinophil response to surgery, the absolute eosinophil level and the per cent change postoperatively, independently, and then combined. Category A, evaluating the per cent change in eosinophils, consists of a postoperative fall in eosinophils of greater than 60 per cent. Category B, evaluating the absolute eosinophil count, consists of a postoperative count of less than 60 eosinophils per cubic millimeter. Category C, evaluating the use of both indices, that is, the per cent change and the absolute level of circulating eosinophils, consists of an absolute postoperative count of less than 60 per cubic millimeter or/and a postoperative fall of greater than 60 per cent. For the "abnormal" eosinophil response to surgery category A consists of two subdivisions: those cases with preoperative counts of less than 60 per cubic millimeter, postoperative counts of less than 60 per cubic millimeter, but per cent change statistically insignificant; and those cases with a preoperative count of greater than 60 per cubic millimeter and a postoperative fall in eosinophils of less than 60 per cent. Category B consists of cases of a postoperative count of greater than 60 per cubic millimeter and category C consists of instances of an absolute eosinophil count of greater than 60 per cubic millimeter with a per cent fall of less than 60 per cent. In the light of the introductory remarks the normal and abnormal eosinophil responses to major surgery are considered equivalent to "adequate" and "inadequate adrenocortical function," respectively. The data are tabulated in Table II. They demonstrate that by the criterion based on per cent change in eosinophils 72 per cent of the patients can be shown to have adequate adrenocortical function. By using the criterion based upon the absolute level of circulating eosinophils 84 per cent of the patients can be shown to have adequate adrenocortical function. Finally by the combined criteria of per cent change in and absolute level of circulating eosinophils 92 per cent of the patients can be shown to have adequate adrenocortical function.

Analysis of the clinical features in the 50 cases studied, that is, the diagnoses, therapies, and postoperative course, for factors known to affect the level of circulating eosinophils or

for evidence suggesting inadequate adrenocortical function, revealed interesting correlations. In categories A and B no significant correlations between adrenocortical or eosinophil related clinical features and the finding of abnormal eosinophil responses could be made except in the 4 cases which were the same 4 cases with abnormal eosinophil responses in category C. All 4 patients in category C with abnormal eosinophil responses revealed some correlations. Their clinical features are shown with the eosinophil data in Table III. In Case 1 the patient was jaundiced with active parenchymal liver damage, due to bile duct obstruction by carcinoma of the pancreas, and he had diabetes for which prolonged insulin therapy preoperatively and postoperatively. He died at home about 4 weeks postoperatively but was not autopsied. After prolonged insulin therapy in psychotics there is a rise in eosinophils which Rud ascribes to the effect of insulin. Also Field and associate demonstrated abnormal eosinophil responses in diabetic patients undergoing surgery; this may possibly have been related to the insulin therapy. Therefore, in this patient the diabetes and insulin therapy may have been responsible for the abnormal eosinophil response. The patient in Case 2 had medical jaundice with active parenchymal liver damage, and postoperatively his progress was poor clinically. Since the postoperative eosinophil response suggested specific therapy, he was treated with lipoadrenal extract for 7 days with marked improvement clinically as early as the first day of therapy. He then failed to improve clinically for the next 4 weeks, and finally readministration of lipoadrenal extract resulted in improvement again and complete recovery. Unfortunately, eosinophil counts and ACTH or epinephrine eosinophil response tests during the period of therapy were not performed. Nevertheless, his response clinically to specific corticoid therapy suggests the possibility of an underlying relative adrenocortical insufficiency manifested by his abnormal eosinophil response to surgery. The patient in Case 3 had a 4 plus Wassermann serological test for syphilis known since early childhood, and he was severely neurotic, and possibly psychotic. He

TABLE II.—EVALUATION OF EOSINOPHIL COUNTS[1] IN MAJOR SURGICAL[3] PATIENTS ON THE FIRST POSTOPERATIVE DAY

Criterion	Total No. cases	Normal eosinophil response: No. cases	Abnormal eosinophil responses*: No. cases	
Category A	50	>—60% (preop. count[2]>60)	14 (28%)	
Per cent[5] change		36 (72%)	Preop. count <60: all postop. counts <60% (But changes insignificant statistically) 10	Preop. count >60: 60% change <—60% 4
Category B	50	<60 eosinophils/cu.mm.	>60 Eosinophils/cu.mm. 8 (16%)	
Absolute count		42 (84%)	Per cent change: <—60% 4	Per cent change: >—60% 4
Category C	50	Absolute count <60/cu.mm. or, and, % change >—60%	Absolute count >60 and per cent change <—60%	
Per cent change and absolute count		46 (92%)	4 (8%)	

*Normal eosinophil response is indicative of adequate adrenocortical function and abnormal eosinophil response is indicative of inadequate adrenocortical function as suggested by the different criterion for each of categories A, B, and C.

[1]Routine laboratory eosinophil count: method of Randolph: No. cells counted is multiplied by factor of 11 to give the cell count per cu.mm. of blood; the fall in eosinophils is recorded as a (—)% change.

[2]Preoperative counts done day before surgery (usually in the afternoon).

[3]Surgery begun in morning with spinal anesthesia, gas, or i.v. barbiturates.

[4]Postoperative counts were done in morning of the first day following the day of surgery.

[5]Per cent change is calculated from a comparison of postoperative to preoperative count; (—) indicating a fall.

was somewhat lethargic and depressed the first day but had an otherwise uneventful postoperative course. Rud demonstrated that patients with psychogenous mental illnesses have a greater coefficient of daily variation of their eosinophils than normal people. Therefore, a possible spontaneous rise in eosinophils may have masked the postoperative fall due to surgical stress in this case. The patient in Case 4 had a hysterectomy during a period of menstruation with a completely uneventful postoperative course. Davis and associate have shown that menstruation is associated with an appreciable fall in eosinophils and this observation suggests the possibility that the

TABLE III.—CLINICAL ANALYSIS OF CASES WITH "INADEQUATE ADRENAL FUNCTION"[1]

Case No. Age, yrs. Sex	Per cent change in eosinophil counts,[2] postop. days 1	2	3	Operation	Diagnosis	Postop. clinical course
1 58 M	−36	−11	+71	Cholecystojejunostomy	Diabetes mellitus. Ca. of pancreas. Jaundice, obstructive with parenchymal damage	Poor postop. course clinically depressed, died at 4 weeks postop. carcinoma of pancreas, carcinomatosis. Rec'd. insulin 10–20 U. preop. and more postop.
2 70 M	−50	+87	—	Laparotomy. Biopsy, liver	Jaundice. Acute hepatitis	Poor clinical response after surgery improved with lipoadrenal extract for 7 days, failure to improve for 4 wks. Repeated specific treatment with improvement again and recovery.
3 34 M	−33	+150	—	Subtotal gastrectomy	Duodenal ulcer. Severe neurotic, possibly psychotic	Lethargic, nervous 1st day postop. otherwise uneventful 4— Wassermann since childhood
4 37 F	−25	+150	—	Hysterectomy	Myoma, uterus. Menstruating endometrium	Uneventful menstruating preoperatively

[1]Absolute eosinophil count greater than 60 and per cent change less than −60 per cent.
[2]− = fall; + = rise.
None of the other patients (50 cases) had any of the following clinical features: poor postoperative course responsive to specific adrenocortical therapy, diabetes, insulin therapy, jaundice, severe neurosis, psychosis, or removal of menstruating uterus.

removal of a menstruating uterus may have been responsible for the abnormal eosinophil response to surgery.

The case of none of the 46 other patients, that is the 92 per cent with adequate adrenocortical function indicated by a first day postoperative eosinophil count of less than 60, or a per cent fall of greater than 60, was complicated by jaundice with active parenchymal liver damage, diabetes, insulin therapy, menstruation, severe neurosis, or psychosis.

Application of the same criteria utilized for the evaluation of the data obtained on the first postoperative day to the second postoperative day also revealed the importance of using the combined criteria of category C. Utilizing 9 of these criteria, 9 of the 48 patients studied or 19 per cent had abnormal responses. Four of the 9 cases were those described in Table III with abnormal first day eosinophil responses; and the remaining 5 patients or 10 per cent revealed no clinical features related to inadequate adrenocortical function or the abnormal behavior of eosinophils. This observation suggests that in 10 per cent of the cases the patients may well have been demonstrating a recovery from the stress of surgery by the second postoperative day, as indicated by the early return of the eosinophil count toward preoperative and higher values; therefore, the resultant falsely abnormal eosinophil responses may be explained by this second day rise. The third day postoperative eosinophil counts revealed an inadequate eosinophil response in 11 of 16 patients by using the same combined criteria of category C. This fact evidently shows that in the majority of cases the adrenocortical eosinophil response to major surgery is not demonstrable by the third day postoperatively.

Therefore the most useful criterion for evaluating the adequacy of adrenocortical function in major surgical patients during the postoperative period as expressed by the eosinophil index consists of an eosinophil count of less than 60 per cubic millimeter; or, if greater than 60 per cubic millimeter, the count must have fallen to at least a level of 60 per cent lower than the preoperative count. When the postoperative count is greater than 60 per cubic millimeter and no preoperative count is available for comparison, or if the eosinophil response is abnormal while the clinical status of the patient is normal, then one can use the ACTH or epinephrine eosinophil response tests to evaluate the actual status of adrenocortical function, and, if necessary, the cortisone eosinophil response test to evaluate the sensitivity of the eosinophil indicator system. The findings for the first postoperative day in terms of the stated criteria for evaluating adrenocortical function indicate the necessity of resorting to the ACTH or epinephrine eosinophil response tests in only 8 per cent or 4 of 50 cases; for the second postoperative day this necessity occurs

in 19 per cent or 9 of 48 cases; and on the third postoperative day it occurs in 70 per cent or 11 of 16 cases. The ACTH, epinephrine, and cortisone eosinophil response tests unfortunately were not performed in this study. In other words, using the criteria based upon the absolute count and per cent change, the eosinophil response to surgery can demonstrate adequate adrenocortical function in 92, 81, and 30 per cent of the patients on the first, second, and third postoperative days, respectively.

No significant correlations between the eosinophil response to major surgery, and the type of anesthesia or surgery, were noted in the 50 cases studied.

DISCUSSION

On the first postoperative day, we were unable to make any significant correlations between the patients with abnormal eosinophil responses and their clinical adrenocortical function or other factors known to affect the level of circulating eosinophils, when using the criteria of per cent change alone and the absolute eosinophil count alone, while such correlations were made in all instances when using both criteria together, that is, the absolute count and/or the per cent change in eosinophils. This fact seems to justify the criteria based upon an absolute count of 60 per cubic millimeter and per cent fall of 60 even through these values were originally arbitrarily chosen.

Since the eosinophil may be the locus of the action of the 11–17 oxyglucocorticoids, in patients with abnormal eosinophil responses to surgical stress there may be an apparent relative humoral insufficiency of 11–17 oxyadrenocorticoids as compared to those patients who exhibit the normal fall in eosinophils. Even though this insufficiency is not apparent clinically in terms of signs and symptoms and the abnormal eosinophil responses may be due to other humoral or subtle unknown factors, is it not possible that the cells of all the body tissues, especially the surgically injured cells, may also be in a humoral environment with relatively insufficient quantities of 11–17 oxyglucocorticoids? Is this apparent tissue cell relative adrenocorticoid insufficiency manifested by metabolic or clinical changes not looked for, or observed, as yet, and are they unfavorable manifestations as is suggested by the similarity of this condition with the eosinophil changes in patients with actual clinical adrenocortical insufficiency? These questions raise biologically significant problems, and it is hoped that further studies will solve them.

In the 2 cases of jaundice with active parenchymal evidence of liver damage, these factors, although associated with other known factors related to adrenocortical function and eosinophil behavior, may have played a role in producing the abnormal eosinophil responses. This is somewhat substantiated by the usual finding of a lymphocytosis in cases of acute infectious hepatitis which suggests that possibly jaundice with active liver damage may be associated with eosinophilia, as circulating eosinophils and lymphocytes tend to vary in the same manner. The analogy may be fortuitous and insignificant especially because of the many other factors involved and the virus nature of acute infectious hepatitis; but it is mentioned at present as it might be a clue to further investigation.

Our findings and interpretations of the level of circulating eosinophils on the second and third day postoperatively are compatible with the findings of Roche and associates. They show that the postoperative eosinophil count occasionally began to rise on the second day and usually rose on the third day. In 13 cases of major surgical patients Field and Marble showed a greater than 50 per cent fall on the second postoperative day in all instances. These more consistent findings for the second day response than the findings in our study may be explained by the fact that their method of counting provided more statistically significant counts as they counted more cells in the counting chamber and used the factor 1.56 to obtain the final count in terms of the number of cells per cubic millimeter of blood. All these findings, with the additional findings of Roche and associates and Laragh and Almy of a profound eosinopenia as early as 3 to 8 hours after the surgical incision, suggest that our criteria for evaluating the eosinophil count in terms of adrenocortical function can be applied usefully and

with reliable significance from 3 to 48 hours after the surgical incision.

An abnormal eosinophil response to surgery with some clinical adrenocortical correlation should be considered an indication for immediate specific 11–17 oxyglucocorticoid therapy on the first and second postoperative days. An abnormal eosinophil response test without clinical adrenocortical correlation should be further studied by epinephrine, ACTH, or cortisone eosinophil response tests and specific therapy instituted depending on the results of these tests.

SUMMARY AND CONCLUSIONS

On patients undergoing major surgery, eosinophil counts were done preoperatively and on the first, second, and third days postoperatively. The counts were made by the clinical pathology laboratory in the daily work routine of the technicians using the direct chamber counting method of Randolph. On the first postoperative day by the criteria based upon the absolute level of and the per cent change in eosinophils, the eosinophil response to major surgery gave excellent correlations with clinical manifestations concerning adrenocortical function and other factors influencing the level of circulating eosinophils (in all 50 cases studied); by either criterion alone, that is the absolute count or the per cent change, the correlations were less significant. On the second postoperative day, by using the same criteria, even less significant correlations were possible, and on the third postoperative day the eosinophil count did not represent any characteristic response to surgery. The criterion most useful for evaluating the adequacy of adrenocortical function in major surgical patients during the postoperative period, as indicated by the normal eosinophil response to surgery, is an absolute eosinophil count of less than 60 per cubic millimeter; or if greater than 60 per cubic millimeter the count must have fallen to at least a level of 60 per cent lower than the preoperative count. When the postoperative count is greater than 60 per cubic millimeter and no preoperative count is available for comparison, or if the eosinophil response is abnormal while the clinical status of the patient is normal, then it is suggested that the epinephrine, ACTH, and cortisone eosinophil response tests can be used to evaluate the patient's adrenocortical function further by laboratory means. Adequate adrenocortical function evaluated by the criteria described for the eosinophil response to surgical stress could be demonstrated in 92 per cent of the patients on the first postoperative day in 81 per cent of the patients on the second postoperative day, and in only 30 per cent of the patients on the third postoperative day. The analyses of the normal and abnormal eosinophil responses revealed some interesting deductions for therapeutic rationale and suggestions for further study.

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GRADED HEPATIC ARTERIAL LIGATIONS IN EXPERIMENTAL ASCITES

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OUR work was undertaken to determine the effect of various degrees of hepatic arterial deprivation on mechanically induced ascites in the dog. The ascites was produced by partial vena caval constriction with a metal band. The nature of the experiment also allowed us to compare differences in the effect of limited, as against massive, hepatica rterial ligations on the physiologic changes accompanying portal hypertension.

EXPERIMENTAL METHODS

Normal healthy adult mongrel dogs were used. Prior to surgery, control chemistry studies were made upon each animal's blood including total protein, albumin-globulin ratio, and serum sodium determinations. In most animals, these determinations were supplemented by serum glucose, alkaline phosphatase, hematocrit, sedimentation rate, blood urinary nitrogen levels, and serum bilirubin studies. All animals were operated upon under intravenous veterinarian nembutal anesthesia. When the thorax was to be opened, intratracheal intubation was carried out and the tube was connected to a positive, alternating oxygen pressure device. Biweekly photographs and blood chemistry determinations were made postoperatively on each animal for 7 months or until death, whichever occurred first. Postoperative care included the daily administration of 300,000 units of penicillin intramuscularly for 1 week. All animals were fed a standard kennel diet.[1]

Blood transfusions were given immediately after surgery when they appeared to be indicated by blood loss or by a drop in systemic arterial pressure. Postmortem studies were made on each animal, and injection studies of the hepatic circulation were photographed in some of the animals.

Forty-one dogs were used in this study and were divided into groups as follows.

Group I (10 dogs). Partial constriction (50 per cent) of the inferior vena cava in the thorax about 3 centimeters above the diaphragm using an aluminum band according to the method of McKee and associates. This group served as a control group and received no other treatment. Vena caval pressures below the band were recorded before and after the band was applied.

Group II (13 dogs). Thoracic caval band plus "*limited*" hepatic arterial ligation consisting of ligation and division of the splenic artery, splenectomy, ligation and division of the hepatic artery, and cholecystectomy (Fig. 1). Removal of the gallbladder and spleen was done only as an ancillary measure to prevent possible necrosis of these organs following the ligations. In 7 of these animals this procedure was done at the same operation as the application of the thoracic caval band. In the other 6 animals the arterial ligations were done 2 weeks after the caval band was in place and ascites was present. Portal vein pressures

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[1]Dog food composition: sodium 0.148 mEq./gram (by our assay); crude protein, not less than 25.00 per cent; crude fat, not less than 4.50 per cent; crude fiber, not more than 5.00 per cent; ash, not more than 11.00 per cent; moisture, not more than 9.00 per cent; nitrogen free extract, not less than 40.00 per cent; vitamin A, 2,000 U.S.P. units per pound; vitamin D, 450 U.S.P. units per pound.

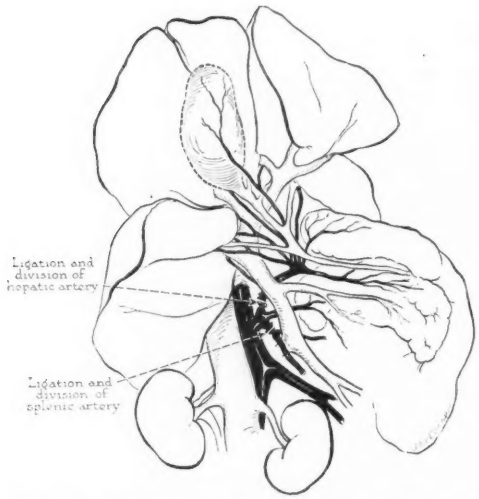

Fig. 1. "Limited" type of hepatic arterial ligation performed upon animals in group II, consisting of ligation and division of the hepatic and splenic arteries. Cholecystectomy and splenectomy were also performed in order to prevent possible necrosis in these organs following the ligations.

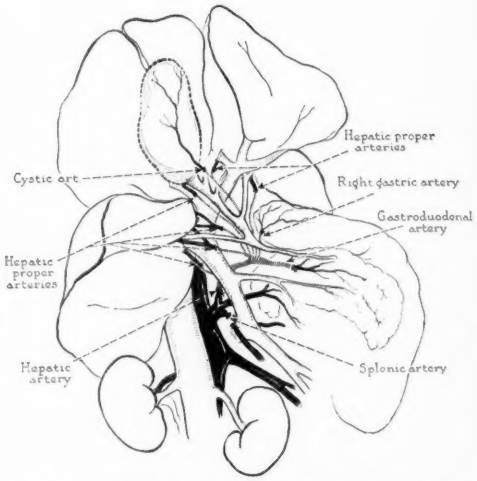

Fig. 2. "Massive" type of arterial deprivation performed upon animals in group III, consisting of ligation and division of the hepatic, splenic, right gastric, gastroduodenal, and hepatic proper arteries with excision of the intervening arterial tree including lymph nodes and fat (cross-hatched area). Splenectomy and cholecystectomy were also done.

were taken before and immediately after splenectomy, again after hepatic artery ligation and cholecystectomy.

Group III (18 dogs). Thoracic caval band plus "*massive*" arterial deprivation consisting of ligation and division of the splenic artery, splenectomy, ligation and division of the main hepatic artery, right gastric artery, gastroduodenal artery and all hepatic proper arteries with removal of the entire intervening segment of tissue containing lymph nodes and small vessels, and finally, cholecystectomy (Fig. 2). The denuded common bile duct and portal vein were the only structures left intact in the area. Since rather remarkable variations in the vascular anatomy in this area were seen, a sketch of the arterial pattern of these vessels was made at the operating table in each case. Some of these sketches are shown in Figure 3. Portal pressure studies were made as in group II. In 10 dogs the procedure was done simultaneously with application of the thoracic caval band, while in 8 dogs the abdominal work was done 2 weeks afterward, when ascites was present. In addition to the usual postmortem studies, injection studies of collateral circulation were photographed.

RESULTS

Pressure studies. Vena caval pressures below the aluminum band rose from an average control pressure of 3.5 centimeters of water to an average of 9.6 centimeters of water after the band was applied. With 50 per cent constriction the pressure in some animals rose as high as 14 centimeters of water. In preliminary studies we found that if the intracaval pressure below the band did not rise to 9 centimeters of water, ascites would usually not develop. Yet, if much more than 50 per cent constriction was made, regardless of caval pressure rise, the animal would usually die within 24 hours from pooling shock. We therefore utilized the 50 per cent constriction as a quantitative guide rather than the caval pressure rise.

Portal vein pressures with this preparation were elevated from an average normal of 12.2 centimeters of water to an average of 20.6 centimeters of water after the development of ascites, the measurements in various

animals ranging from 15.6 to 24 centimeters of water.

In group II animals (splenectomy, limited hepatic artery ligation, and cholecystectomy 2 weeks after the thoracic caval band was applied), portal pressures dropped an average of 2 centimeters of water (from 20.6 to 18.5 cm. water) after splenectomy, and an additional average drop of 4 centimeters of water (from 18.5 to 14.4 cm.) after hepatic artery ligation.

In group III animals (splenectomy and massive vascular deprivation of hepatic blood supply with cholecystectomy 2 weeks after the thoracic caval band was applied), portal pressures dropped an average of 2 centimeters of water after splenectomy, and an additional 6.2 centimeters (from 18.5 to 12.3 cm.) after the arterial deprivation. Thus, the additional vascular ligations in group III resulted in a further 2 centimeter portal pressure drop as compared with that following the limited vascular ligation in group II. It should be mentioned that femoral arterial blood pressures did not alter from preligation levels, so that in neither group could the diminution in portal pressure be attributed to a drop in systemic arterial pressure.

In a few of the animals which failed to form ascites the thorax was reopened at a later date and the vena cava was completely constricted, then ligated and actually severed. Two animals with the vena cava severed developed ascites afterward, and were treated with ligation operations. In these animals, 21 days after the inferior vena cava was ligated and divided in the thorax, the portal pressure averaged 23.5 centimeters of water. After splenectomy this pressure reading did not change. However, immediately after ligation of the hepatic artery it dropped to 20.4 centimeters of water. Two months (58 days) after splenectomy and ligation of the hepatic artery the portal pressure was 18 centimeters of water, and remained at this same value for 5½ months, despite the absence of ascites.

Ascites accumulation. In the group I animals (thoracic caval band only) the pattern of ascites accumulation was rather constant. In 2 weeks 1,500 to 4,000 cubic centimeters of ascitic fluid had accumulated. If the fluid

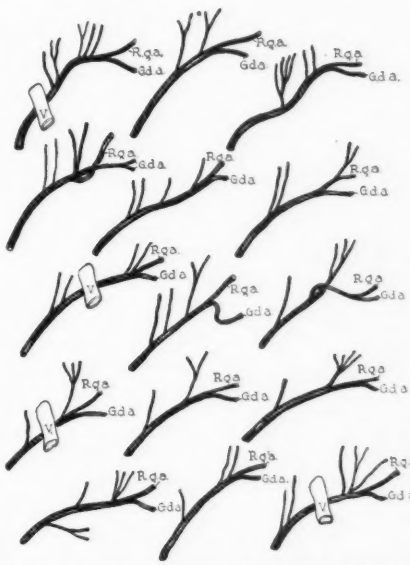

Fig. 3. Examples of variations in anatomy of the hepatic artery and its branches in the dog, redrawn from sketches made at surgery. *R.g.a.*, right gastric artery; *G.d.a.*, gastroduodenal artery; *V.*, portal vein.

was removed at this time, a full reaccumulation occurred in another 2 weeks. It can be said that an animal with a thoracic caval band will, as a rule, form ascites at an average rate of about 3,000 cubic centimeters every 2 weeks, provided the fluid is removed at such intervals. Occasionally, no ascites developed after placement of the thoracic band. Such animals could not be included in the control group, since the pattern of ascites formation was to be followed. The portal pressures in animals which failed to develop ascites were only mildly elevated, never reaching the levels of those animals which later developed ascites. Our assumption, based on observations in these animals, was that the reason for the failure to develop ascites was the presence of collateral venous channels which by-passed the vena caval band and negated its effect.

The pattern of ascites formation was determined by observations over a 7 month period. Generally, a rather full ascites developed gradually in 2 weeks and did not subside spontaneously for periods ranging from 4 to 7 months, if the animal survived (see Table I).

TABLE I.—DOG NO. 139. GROUP I, PARTIAL CONSTRICTION INFERIOR VENA CAVA IN THORAX (CONTROL)

Date	Operation	Total protein	Albumin	Globulin	Sodium	Ascites*	Weight
6-27-51	Vena cava constriction	7.0	2.7	4.6	136	0	25
7-13-51	Abdominal exploratory	5.15	2.65	3.5	148	3000	30
7-25-51		5.3	2.75	2.55	135	+	
8- 9-51		5.7	2.7	3.0	145	++++	
8-22-51		5.1	2.75	2.35	147	++++	27.5
9- 4-51		5.8	3.3	2.5	152.5	++++	
10- 9-51		6.6	2.95	3.75	143.5	++++	
11- 6-51		6.2	2.55	3.65	161	++	
12-11-51		6.4	3.35	3.05	163	0	
12-19-51		5.6	3.1	2.5	164	+	22
1-22-52		5.9	3.4	2.5	157.5	0	
3-18-52		5.9	2.95	2.95	151	0	
5- 5-52		7.0	2.0	4.1	156.5	0	22

*Based on correlation studies: +=500 c.c., ++=1,000 c.c. to 1,500 c.c., +++=2,000 c.c. to 2,500 c.c., ++++=3,000 c.c.

No alteration in standard diet was allowed, but there was obviously some variation in quantity of intake from day to day depending upon the animal's appetite.

Although a few dogs developed ascites somewhat slower, the average time interval for the development of a full blown ascites was 17 days. Six of the control animals were observed for as long as 1 year. In 2 animals ascites of maximum magnitude was noted to remain longer than 7 months. During the development of ascites all animals appeared rather emaciated and underwent drastic changes in blood chemistry which will be discussed later.

Five of 7 dogs in group II with simultaneous band and limited ligation procedures survived. All developed ascites at a slower rate, averaging 23 days, as compared with the 17 day average in the untreated group I animals. The ascites lasted from 1 to 4 weeks, then all but disappeared for 6 to 10 days, only to reappear for 2 to 4 months. The last subsidence period corresponded closely to the time of spontaneous disappearance of ascites in the untreated animals in group I (see Table II).

Six of 7 additional dogs survived in group II, with limited ligation delayed until a full blown ascites was present. The effect of the ligation procedure in these animals was most disappointing. Ascites was seen to develop in from 5 to 12 days, averaging 10 days, from the date of operative paracentesis and the ligation procedure. This period of reaccumulation of ascites was thus actually shorter than the average of 17 days for the initial formation of maximum ascites (see Table III). Furthermore, the ascites lasted 4 to 6 months except in 2 instances in which the ascites disappeared with the onset of mange, 2 months and 3 months after surgery, respectively.

In summarizing animals in group II, we are able to say that a limited type of hepatic artery ligation, although accompanied by splenectomy and cholecystectomy, did not prevent ascites either in the immediate or delayed group. However, there was more of an effect on the pattern of accumulation of ascites when the ligation was done simultaneously with the application of the thoracic caval band, than there was following the delayed type of ligation.

In group III animals (massive type of hepatic arterial excision with splenectomy and cholecystectomy) in which this procedure was done simultaneously with the application of the thoracic caval band, the pattern of development of ascites was altered rather remarkably in the dogs surviving the procedure. Four out of 10 dogs survived in this group and in each instance ascites was completely, or almost completely, prevented. The pattern

TABLE II.—DOG NO. 173. GROUP II, SIMULTANEOUS PROCEDURE CONSISTING OF VENA CAVA CONSTRICTION AND "LIMITED" HEPATIC ARTERY LIGATION

Date	Operation	Total protein	Albumin	Globulin	Sodium	Ascites	Weight
10- 9-51		7.4	5.0	2.4	147.5	0	32
10-15-51	Simultaneous vena cava constriction and "limited" hepatic artery ligation						
10-23-51		5.2	3.1	2.1	155	0	
11- 6-51		4.95	2.75	2.2	166	++++	26
11-12-51						+++	
11-15-51						+	23
11-20-51		5.5	3.4	2.1	164	++	
11-27-51						0	
12- 4-51		6.1	3.7	2.4	167.5	0	22
12-19-51		4.95	3.25	1.7	164	0	
1- 4-52		5.3	3.4	1.9	174	0	
1-15-52		3.8	2.5	1.3	173	0	27
1-22-52						+++	
1-30-52						++++	
2- 5-52		4.8	2.88	1.2	155	++++	21
2-26-52		5.0	2.55	2.45	164	++++	
3-11-52		4.95	2.45	2.5	153	++++	
5- 5-52		6.45	3.9	2.55	162.5	++++	
5-19-52						++	24
5-29-52						0	
6-11-52		7.0	4.8	2.2	151	0	28

in these 4 animals was about the same. A small amount of ascites developed shortly after surgery and lasted for a few days to a month and then subsided, with no further ascites up to 7 months of follow-up observation (see Table IV).

In the group III animals with massive arterial deprivation performed 2 weeks after application of the vena caval band, 4 out of 8 dogs survived the full observation period. In 3 of these animals there was a moderate or small degree of ascites for periods ranging from 5 days to 3 weeks, after which there was no ascites, or a 1 plus or 2 plus accumulation, which lasted for periods up to 10 days to 2 weeks. The ascites then disappeared again only to reappear after 6 weeks, again for a few days. This pattern recurred on a more or less cyclic basis over a 7 month period (see Table V). The fourth surviving animal also followed this same type of cyclic course, but with a greater ascites. After 7 months a 3 plus ascites remained in this animal.

Blood chemistry studies. Typical examples of blood chemistry determination in dogs from each group are shown in Tables I to V. In group I animals with constriction of the thoracic vena cava only, the general trend was for the blood protein level to diminish and for the serum sodium level to increase with the development of ascites. In the treated animals of groups II and III, the very slight increment in serum sodium levels in some animals and the actual decline in these levels in others, while a full-blown ascites existed, prompted us to do excretory sodium studies on several animals. In each instance we found that the excretion of sodium dropped precipitously with the development of ascites. Thus, the almost normal serum sodium levels in some ascitic animals actually represented a state of sodium retention. Further study of this phase of the work will be presented at a later date.

In all groups the plasma protein levels reflected fairly well the state of depletion of the

TABLE III.—DOG NO. 183. GROUP II, DELAYED "LIMITED" HEPATIC ARTERY LIGATION IN ASCITIC DOG

Date		Total protein	Albumin	Globulin	Sodium	Ascites	Weight
11–13–51	Thoracic caval band	7.4	3.2	4.2	165	0	27
11–27–51		5.25	3.05	2.2	156.5	++++	24
11–29–51	"Limited" hepatic artery ligation, 225 c.c. blood transfusion					3000 cc.	
12– 4–51						0	
12–11–51		5.95	2.95	3.0	160	+++	23
12–19–51		5.1	4.05	2.35	164	+++	
12–21–51						++++	20
1– 8–52		6.4	4.05	2.35	164.5	++++	
1–22–52		6.1	3.2	2.9	160	+++	
2– 6–52		6.01	3.24	2.77	146.5	+++	21
3– 4–52		5.3	2.45	2.85	160.5	+++	
5– 5–52		6.5	2.8	3.7	153.5	+++	
6–11–52						++++	10

blood due to the ascites. When a greater degree of ascites was present, the plasma proteins were very low, in some instances approaching 50 per cent of control levels. When less or no ascites was present, the plasma proteins were rather normal, provided the animal was eating. Ligation of hepatic arterial vessels, whether limited or massive, appeared to have only an indirect effect upon plasma protein levels, the levels being determined by the presence or absence of ascites and by the protein intake.

Despite the fact that the protein content of the diet was not increased at any time, plasma protein levels spontaneously returned to normal as ascites was absorbed. The only exception was when paracentesis actually removed ascitic fluid from the animal's body. Thus, it would appear that the animals were able to utilize the protein content of their ascitic fluid, once it returned to the blood.

We have found, as have others, that limited types of hepatic arterial ligation are not, as a rule, accompanied by marked functional hepatic damage. However, in our experience, animals with massive arterial deprivation suffered proportionate hepatic functional damage. In such animals the alkaline phosphatase levels rose rather remarkably, even in dogs destined to recover (see Tables IV and V). Moderate increases were also noted in the serum glucose and serum bilirubin in most animals in this group. Gross jaundice was seen only in 3 animals. All animals lost considerable weight in the postoperative period, whether the ligations were limited or massive. However, weight loss in these animals was no more than in the control ascites group without hepatic arterial ligations.

Mortality. In the control animals comprising group I, only those dogs which survived for a long enough period to observe the total course of the ascites accumulation and absorption were utilized. However, the mortality, calculated on the basis of all animals operated upon as group I animals, was 12.5 per cent. Causes of death in this group included such unrelated conditions as distemper and mange, while in a few instances death occurred within 24 to 48 hours after application of the band, presumably from pooling shock. In 1 instance death occurred due to pulmonary embolism and gangrene of the lung 5 weeks after the application of the band. Postmortem examination in this animal revealed that the embolism arose from a thrombus which occurred at the site of the vena caval constriction.

Mortality in group II animals in the simultaneous group was 2 out of 7, or 28.5 per cent, while the mortality in this group in which the delayed procedure was done was 1 out of 6,

TABLE IV.—DOG NO. 215. GROUP III, SIMULTANEOUS PROCEDURE CONSISTING OF VENA CAVA CONSTRICTION AND "MASSIVE" HEPATIC ARTERY EXCISION

Date	Operation	Total protein	Alb.	Glob.	Sod.	Alk. phos.	Serum glucose	B.U.N.	Serum bilirubin	Ascites	Weight
4- 8-52	Simultaneous vena cava constriction and "massive" procedure, 200 c.c. blood	6.3	2.6	3.7	149	3.3	77	16.4	0.4	o	58
4-11-52		5.5	2.7	2.8	168	19.6	78	17.1	0.25	o	46
4-15-52		4.8	2.8	2.0	159	15.2	64	20.0	0.2	+	43
4-18-52										++	
4-23-52		3.7	2.3	1.4	161	11.65	88	15.5	0.2	++	34
5- 2-52										+++	
5- 6-52		6.5	2.8	3.7	155.5	11.0	74.8	21.2	0.13	+++	24
5-19-52										+	
5-29-52										o	
6- 9-52		6.1	3.4	2.7	152.0	2.75	68	26.0	0.2	o	31
8-26-52										o	48

TABLE V.—DOG NO. 200. GROUP III, DELAYED "MASSIVE" HEPATIC ARTERY EXCISION IN ASCITIC DOG

Date	Operation	Total protein	Alb.	Glob.	Sod.	Alk. phos.	Serum glucose	B.U.N.	Serum bilirubin	Ascites	Weight
3-18-52		7.6	2.5	5.1	151	2.2	34	16.6		o	44
3-20-52	Thoracic caval band										
4- 7-52		4.5	2.35	2.15	150	1.6	90	20.8	0.2	++++	38
4- 8-52	Massive procedure									4000 cc.	
4-11-52		4.95	2.65	2.30	163	5.9	78	12.3	0.1	o	25
4-15-52		4.9	2.45	2.45	152	10.4	65	15.6	0.35	+	21
4-16-52	200 c.c. blood transfusion										
4-23-52		6.5	2.45	4.05	140.5	25.7	67	11.5	0.3	++	25
5- 2-52										o	
5- 6-52		7.5	2.4	5.1	148.5	16.2	74.8	13.8	0.25	o	33
5-19-52										++	
5-29-52										+	
6- 9-52		8.8	2.6	6.2	159.5	1.5	53	19.2	0.12	+	34
7-10-52										o	
8-26-52										o	35

or 16.6 per cent. Thus, the combined mortality with limited ligation was 23 per cent. The 2 deaths in the simultaneous group occurred within 72 hours after surgery, and since there were no unusual postmortem findings the deaths were ascribed to pooling shock. A third dog in this group died 10 months after surgery with a large bleeding gastric ulcer. We cannot be sure whether this lesion is related in any way to the limited hepatic artery ligation, nor that death was due to the ulcer. The animal was markedly emaciated and had a 3 plus ascites at the time of death. The 1 death in the delayed group II was apparently due to shock shortly after surgery, since this animal's blood pressure dropped rather precipitously and the animal expired before a blood transfusion could be given.

The mortality in group III animals was considerably higher. In the animals with the simultaneous procedure, 6 of 10 dogs died, a

Fig. 4. Necrosis of the liver resulting from massive arterial deprivation of the liver.

mortality of 60 per cent. The mortality of animals with the massive ligation delayed for 2 weeks was 50 per cent. Thus, the overall mortality in animals with massive arterial deprivation, both immediate and delayed, was 55.5 per cent. Four of the 6 deaths in the simultaneous group with massive arterial deprivation can be attributed to liver damage. The earliest of these deaths occurred in 48 hours, and may have been caused partially by heart failure. However, the liver had a mottled appearance, and postmortem injection studies revealed almost no gross collateral arterial channels to the liver. The second death occurred in 4 days, apparently from physiological liver damage. Serum alkaline phosphatase levels in this animal rose from a preoperative level of 1.6 to 86.4 milligrams per cent before death. The third death occurred 16 days postoperatively and was caused by massive necrosis of the liver (Fig. 4). Injection studies in this animal also revealed a paucity of collateral channels (Fig. 5). The fourth death, presumably from liver damage, occurred after 3 weeks. The liver was mottled at postmortem examination. The animal had lost 10 pounds (¼ of its body weight) in the 3 weeks prior to death. Of the 2 deaths not due to demonstrable liver damage, one occurred the day of surgery and was attributed to shock, while the other occurred 3 weeks after surgery and was due to bilateral pneumonia with bilateral hydrothorax. In this animal there was only a 1 plus ascites present at the time of death.

Fig. 5. Postmortem injection specimen from the same animal as Figure 4, showing the left inferior phrenic artery as a large vessel. However, in this case there was not sufficient anastomosis with the right side of the diaphragm to permit survival of the liver.

Analysis of the 4 deaths in the group of 8 animals with delayed massive arterial deprivation revealed that 2 of these animals became deeply jaundiced after 3 weeks and both died 4 weeks after surgery with almost identical perforated duodenal ulcers located opposite the orifice of the ampulla of Vater. The massive excision of vessels together with the supporting structures of the duodenohepatic ligament had apparently allowed the common bile duct to become kinked, resulting in obstructive jaundice and the ulcers. The ducts were patent to probing. This type of ulcer is commonly produced in dogs by ligation of the common duct. Neither of these dogs had any ascites at the time of death, although at the time of the arterial deprivation operation a 4 plus ascites had been present. The other 2 deaths were from intercurrent infection, 2 months and 5 months after surgery.

Postmortem injection studies in the various animals revealed 6 traceable sources of collateral hepatic blood supply. These were the left inferior phrenic artery, fine vessels in the gastrohepatic ligament and along the common duct, the right superior phrenic artery, right inferior phrenic artery, a fibrillary network on the inferior vena cava, and fine vessels in the hepatorenal ligament (see Fig. 6).[1]

DISCUSSION

The basic studies of Markowitz, Rappaport, and Scott, and simultaneously those of Davis, Tanturi, and Tarkington, showed that antibiotic therapy reduced the mortality of hepatic artery ligation. These studies laid the groundwork for the employment of arterial ligations of the liver as a therapeutic tool. Subsequently, considerable experimental work was done to establish the fact that although antibiotic therapy lessens mortality following limited types of arterial ligations of the normal liver, the more drastic arterial deprivations result in liver necrosis and death despite antibiotic therapy. Under such circumstances, survival appears to be directly proportional to the degree of collateral arterial supply available. Thus, the liver is no different from other organs in this regard. For example, it is well known that antibiotic therapy will allow the intestine to survive remarkably well on borderline levels of viability by preventing an overwhelming invasion by bacteria either until new blood vessels form, or until already existing vessels can carry more blood. When insufficient blood supply remains, however, to support even a diminished state of physiologic performance in any organ, necrosis must supervene whether antibiotics are used or not.

Our results are in close accord with those of Grindlay and of Thors who have independently demonstrated phenomena corollary to our findings. They showed that ligation of the hepatic artery alone in normal and cirrhotic dogs produced little change in either

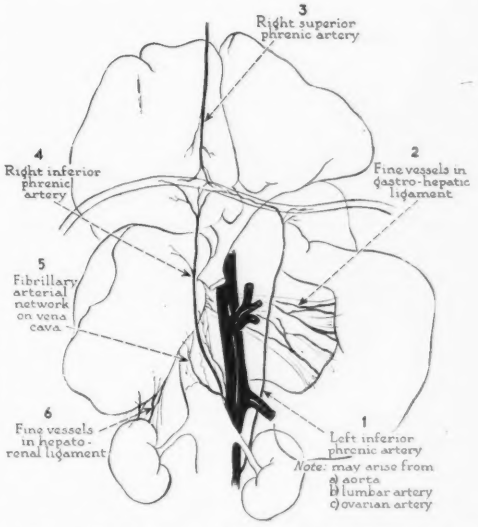

Fig. 6. Main sources of collateral blood supply to the liver of the dog as demonstrated by postmortem injection studies. All of the collaterals were not present in each instance.

hepatic vein pressure or in oxygen saturation of hepatic vein blood. When, however, all hepatic artery branches were ligated, there was a significant decrease in both the pressure and oxygen saturation of hepatic vein blood. Our results indicate that ascites accumulation cannot be prevented when only the hepatic artery is ligated, but can be prevented in surviving animals when all of the main hepatic arterial supply is severed. Therefore, it would appear that there is a direct relationship, or at least a parallelism, between the formation of ascites on the one hand and the pressure and oxygen saturation of hepatic vein blood on the other. We are aware that ascites, once formed, is perpetuated by a combination of many functional factors, including endocrine, renal, cardiodynamic, local vascular, and nutritional. Yet, it has been demonstrated both clinically and experimentally that the cycle of ascites accumulation can be broken, within certain limits, by an alteration in only one of the factors—e.g., the local vascular factor.

The question might well be raised as to whether a procedure which causes a marked

[1]Since completion of our work, an article has appeared which described some of the collateral arterial supply to the dog's liver (JEFFERSON, N.C., PROFFITT, M.M., and NECHELES, H. Collateral arterial circulation to the liver of the dog. Surgery, 1952, 31: 724-730).

diminution in arterial blood supply to an already hypoxic organ is an "unphysiologic" one. Our dogs with a massive arterial deprivation all showed great increases in alkaline phosphatase levels. Fraser and coworkers showed that massive hepatic arterial ligation in normal dogs resulted in a 65 per cent mortality despite penicillin therapy. This figure corresponds closely with our own 55 per cent mortality in ascitic dogs. Two-thirds of their surviving animals exhibited a marked liver insufficiency which lasted an average of 12 days, after which the liver function tests returned to normal. Hence it appears that in most instances deprivation of the main hepatic blood supply, if it does not cause death, does result in parenchymal damage, at least until such time as enough blood supply becomes available to restore a reasonable level of physiologic function.

We believe that the variability in results obtained with hepatic arterial ligation in human cirrhotic patients can be explained by drawing a parallel between our results in dogs and the human dissection studies of Michels. We found a surprising variability in the direct and collateral blood supply to the dog's liver (Fig. 3), and Michels has shown even more remarkable variations in the anatomy of the arterial vasculature in man. In fact, the latter is so extreme that one wonders whether the therapeutic results of a standard ligation operation can ever be predicted.

If we examine the hepatic arterial ligation procedure as it is being done in cirrhotic patients, we find that Berman (1) ligates the hepatic artery *proximal* to the gastroduodenal artery in addition to the splenic and left gastric arteries, while Rienhoff ligates the hepatic artery *distal* to the gastroduodenal artery in addition to the splenic artery. These variations appear to be relatively unimportant, since both leave a fair degree of collateral circulation in most instances. However, deaths due to liver necrosis have been reported following even these limited types of hepatic arterial ligation. Berman and Hull (2) have reported both clinical and laboratory data showing that ligation alone is not as efficacious in the treatment of ascites as is ligation supplemented by low sodium diet or exchange resin therapy. Berman and Hull (3) have further shown that the fall in blood pressure resulting from hepatic arterial ligation in hypertensive cirrhotic patients may be sufficient to throw the patient into a state of liver failure. In such cases the hepatic cells are apparently dependent upon the hypertension to sustain their viability, and therefore Berman believes hypertension to be a contraindication for hepatic artery ligation. In Madden's recent series of hepatic arterial ligations in cirrhotic patients, only 1 out of 7 showed a beneficial result.

Thus, we see the two extremes resulting from the same type of ligation: on the one hand, insufficient collateral circulation to maintain viability of the liver, while on the other hand, sufficient collateral blood supply to permit the reaccumulation of ascites. Somewhere between these extremes are the cases which fall within the therapeutic range of limited ligation by virtue of an optimum collateral blood supply. The reported success of the procedure in some hands indicates that this range is by no means inconsequential.

We have shown that in dogs the collateral circulation of the liver is great enough to render anything less than a "massive" excision ligation so incomplete as to be almost ineffective in preventing the recurrence of ascites. Our evidence suggests, therefore, that within certain limits, the more extreme the arterial deprivation of the liver, the better the protection against the formation or re-formation of ascites. On the other hand, the greater the arterial deprivation of the liver, the higher the mortality.

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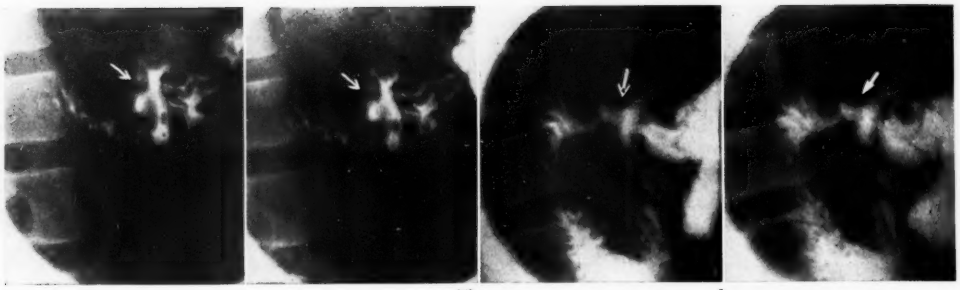

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Fig. 1.

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Fig. 2.

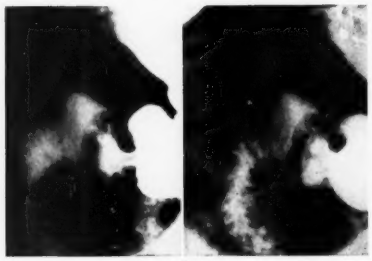

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Fig. 2.

Fig. 1. a, J. D., 47 year old male, was operated upon in December 1950 for chronic cholecystitis and cholelithiasis. A few days before operation these roentgenograms were taken showing a large, spastic, constantly deformed, and irregular duodenal cap. An ulcer was noted at operation. b, Some 2 years later the repeat roentgenograms showed a smooth constriction of the apex of the duodenal cap but no active ulcer. The patient has been treated for this ulcer and his symptoms have subsided markedly.

Fig. 2. a, B. G., a 46 year old male, was operated upon in October 1950 for chronic cholecystitis and cholelithiasis. Several weeks prior to surgery these roentgenograms showed a niche on the superior border of the duodenum suggesting an ulcer. This finding was confirmed at operation. b, Repeat roentgenograms 20 months later showed a normal duodenum. The patient was completely free of symptoms.

Cholecystectomy and Its Relation to the Stomach and Duodenum; Review of 75 Cases with Preoperative and Postoperative X-ray Studies.—Robert E. Rothenberg.

CHOLECYSTECTOMY AND ITS RELATION TO THE STOMACH AND DUODENUM

Review of 75 Cases with Preoperative and Postoperative X-ray Studies

ROBERT E. ROTHENBERG, M.D., F.A.C.S., Brooklyn, New York

THE persistence or recurrence of gallbladder symptoms after cholecystectomy presents an unsolved challenge to the surgeon and constitutes a source of great discomfort to the patient. Interstitial pancreatitis, reflux of bile into the pancreatic duct, the cystic duct stump syndrome, severe pylorospasm, and repeated tonic spasm of the sphincter of Oddi have all, at various times, been labelled as the cause of this unhappy phenomenon.

In an attempt to learn more about the nature of postcholecystectomy symptoms, 75 patients suffering from cholecystitis and cholelithiasis were subjected to roentgenographic studies of stomach and duodenum prior to removal of the gallbladder. The x-ray studies were then repeated in all cases some 6 months to 2 years after cholecystectomy. The group consisted of 54 females and 21 males. No attempt was made to select cases and every patient who submitted to the preoperative and postoperative x-ray studies has been included. There were, however, several patients with acute cholecystitis who had received no preoperative roentgenograms of the stomach and duodenum and they, therefore, have been excluded from this study. Because the gallbladder and duodenum lie in such close proximity anatomically and because the duodenal ulcer syndrome is often associated with chronic calculous cholecystitis, it was thought that the status of the duodenum before and after surgery would bear closer investigation. It was hoped to learn whether duodenal irritability, duodenal distortion, or duodenal ulcer played a role in the production of postcholecystectomy symptoms.

There were 6 patients, 5 males and 1 female, who, in addition to suffering from chronic calculous cholecystitis, gave histories which were highly suggestive of an accompanying duodenal ulcer. The preoperative roentgenographic studies of the stomach and duodenum showed various evidences of ulcer formation and the operative findings confirmed the x-ray observations. Since the paramount symptomatology in these patients was that of biliary

From the Department of Surgery of the Central Medical Group of Brooklyn.

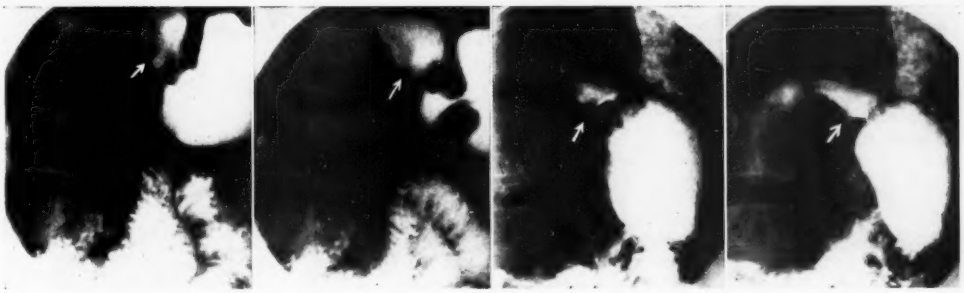

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Fig. 3. a, G. S. G., a 34 year old female, was operated upon for chronic cholecystitis and cholelithiasis in September 1951. A few days previously these roentgenograms showed a smooth niche thought to be due to an inactive ulcer. b, Repeat roentgenograms 10 months after cholecystectomy showed a healing but persistent niche. The patient still has symptoms suggestive of an active ulcer.

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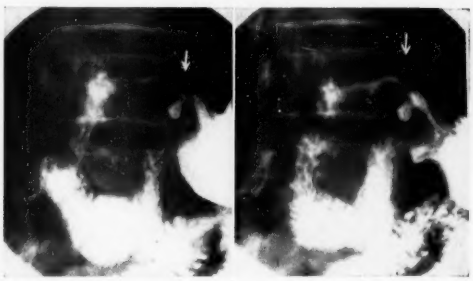

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Fig. 4. a, A. D. B., a 38 year old male, was operated upon in April 1949 for chronic cholecystitis and cholelithiasis. Roentgenograms of the stomach and duodenum taken a month previously showed a typical duodenal ulcer with a constricted, irregular, nonfilling duodenal cap. This finding was confirmed at operation. b, Another study 22 months later revealed the ulcer still to be present. The patient had marked symptoms from his ulcer and could not be aided through medical management. Accordingly, a subtotal gastrectomy was performed.

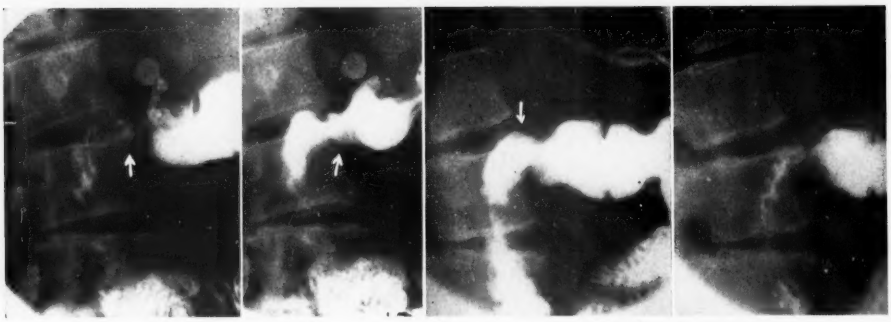

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Fig. 5. a, M. I., a 54 year old male, was operated upon in November 1948 for a chronic cholecystitis and cholelithiasis. Six weeks prior to surgery roentgenograms showed a duodenal cap which was spastic and revealed a defect suggestive of an ulcer. An ulcer was noted along with the cholecystitis at operation. b, Two years after cholecystectomy repeat roentgenograms showed a smooth constriction of the duodenum which was thought to be due either to a healed ulcer or to adhesions from the operative procedure. The patient, however, continues to have symptoms suggestive of activity of duodenal ulcer.

colic, cholecystectomy alone was carried out. Postoperatively, these patients were treated medically for their ulcers with improvement of symptoms occurring in 4 cases. One patient did not respond at all to medical management and it was necessary to perform a subtotal gastrectomy 2 years after cholecystectomy. The sixth patient continued with moderate ulcer symptoms despite medical management. The postcholecystectomy roentgenograms of the stomach and duodenum in these patients showed some duodenal deformity, but there were evidences of healing in all but the male patient who required gastrectomy. None of the patients who were studied in this group demonstrated any postcholecystectomy symptoms such as colic or biliary dyskinesia (Figs. 1 to 6).

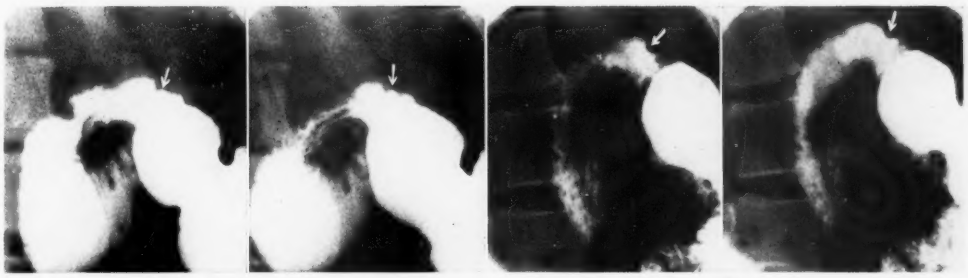

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Fig. 6. a, A. W., a 49 year old male, was operated upon in October 1950 for an acute exacerbation of a chronic cholecystitis with cholelithiasis. Roentgenograms of the stomach and duodenum taken just a few days previously showed marked 5 hour gastric retention and a niche in the duodenal cap near its base, which was diagnosed as a duodenal ulcer. b, Repeat roentgenograms which were taken 18 months later showed the same small niche in the duodenum. The patient has mild symptoms referable to the ulcer.

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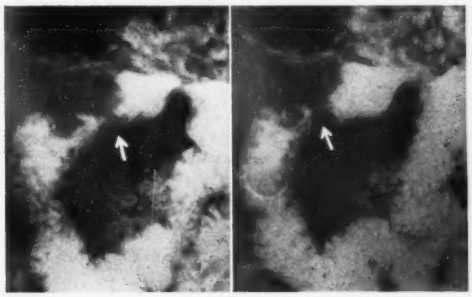

b

Fig. 7. a, W. F., a 59 year old male, was operated upon in October 1949 during an acute exacerbation of a chronic calculous cholecystitis. Roentgenograms of the stomach and duodenum taken some 5 months previously were normal. No duodenal pathology was noted at operation. b, Roentgenograms taken 6 months after cholecystectomy showed a constriction of the duodenum just beyond the cap. This was interpreted either as an ulcer or as a deformity due to postoperative adhesions. This patient has no acute symptomatology.

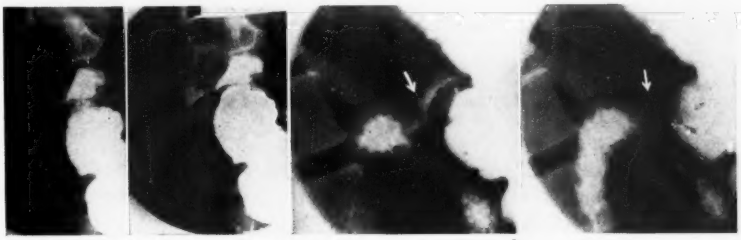

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Fig. 8. a, C. C., a 40 year old male, was operated upon in July 1949 for chronic cholecystitis and cholelithiasis. Roentgenograms taken a few days prior to operation showed a normal stomach and duodenum. No duodenal pathology was noted at surgery. b, Repeat roentgenograms 2½ years after cholecystectomy showed an irritable nonfilling duodenal bulb suggestive of an ulcer. The patient, however, does not have ulcer symptoms and is in good health. His only complaint is occasional heartburn.

a

b

Fig. 9. a, F. H., a 50 year old female, was operated upon in December 1949 for chronic cholecystitis with cholelithiasis. Roentgenograms taken a week previously showed a normal stomach and duodenum. No duodenal pathology was noted at operation. b, Roentgenograms taken 6 months after cholecystectomy showed a constriction of the duodenum near the apex of the cap, suggestive either of an ulcer or caused by adhesions from an operative procedure. The patient is in excellent health and has no symptoms.

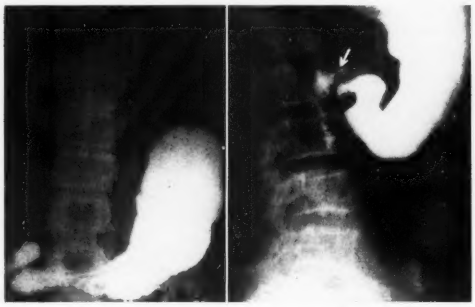

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Fig. 10. a, A. K., a 54 year old male, was operated upon in April 1950 for chronic cholecystitis with cholelithiasis. A month before surgery roentgenograms revealed a normal stomach and duodenum. No duodenal pathology was seen at operation b, Repeat roentgenograms 8 months after cholecystectomy showed the duodenal cap to be spastic and to be irregular at its base. This was thought to be due either to an ulcer or to adhesions from his operation. The patient has no ulcer symptoms and is in good health.

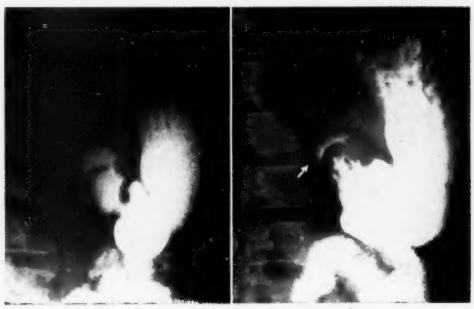

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Fig. 11. a, M. A., a 37 year old female, was operated upon in August 1950 because of chronic calculous cholecystitis. A week prior to surgery roentgenograms showed a normal stomach and duodenum. At operation, no duodenal pathology was noted. b, Repeat roentgenograms 22 months after cholecystectomy showed a nonfilling, spastic, irregular duodenal cap strongly suggesting an ulcer. The patient, however, is completely free of symptoms and is in the best of health.

A most interesting finding was noted in 8 patients whose roentgenograms showed normal stomach and duodenum prior to cholecystectomy but who, some 6 months to 2½ years after removal of the gallbladder, displayed deformities and distortions of the duodenum suggestive of ulcer. Repeated films were taken of the duodenum in all of these 8 cases and the deformity was proved to be a constant finding. No duodenal pathologic condition had been noted on direct inspection at operation. Close questioning revealed that these patients were enjoying good health and all of them denied having any symptoms which might be attributed to duodenal ulcer or duodenal irritability. These findings lead one to believe that the duodenal distortion seen on the x-ray film was the direct result of the

a

b

Fig. 12. a, E. M., a 41 year old male, was operated upon in August 1950 for chronic cholecystitis and cholelithiasis. Roentgenograms taken 2 weeks before operation showed a normal stomach and duodenum. b, Roentgenograms taken 22 months after cholecystectomy showed a smooth constriction in the prepyloric region suggesting an old or healing ulcer. The patient, however, is completely without symptoms and is in good health.

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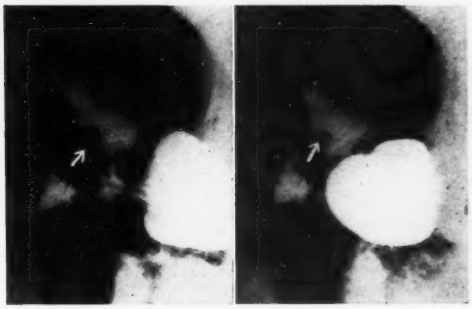


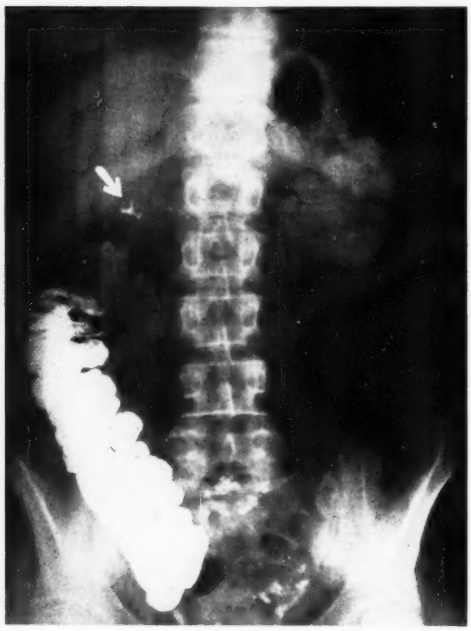
b

Fig. 13. a, O. Z., a 41 year old female, was operated upon in December 1950 for a chronic calculous cholecystitis. Six weeks previously, roentgenograms of the stomach and duodenum were found to be normal. No duodenal pathology was noted at operation. b, Roentgenograms 6 months after cholecystectomy revealed a smooth depression on the posterior border of the duodenal cap which was thought to be due to an old, healed ulcer. The patient, however, was completely free of symptoms referable to the gastrointestinal tract.

cholecystectomy. Raw surfaces are left behind following removal of the gallbladder, and exudate in the region of Morrison's pouch frequently follows procedures of this kind. The repair of raw surfaces and the absorption of exudate probably lead to the formation of adhesions with resultant distortion of the adjacent duodenum. None of the patients in this group had any postcholecystectomy symptoms such as pain, colic, or biliary dyskinesia (Figs. 7 to 14).

The remaining 61 patients had normal gastric and duodenal x-ray findings both before and after cholecystectomy. No duodenal disease had been noted on direct inspection at operation. Despite these normal findings, there were 6 patients, all women, who had severe postcholecystectomy symptoms. Colic-

a b



c

Fig. 14. a, M. G., a 41 year old female, was operated upon in March 1951 for chronic cholecystitis with cholelithiasis. Four months prior to operation, roentgenograms showed a normal stomach and duodenum. No duodenal pathology was seen at surgery. b, Repeat roentgenograms 1 year after cholecystectomy showed a small niche in the duodenal cap near the apex, suggesting an ulcer. b, Roentgenograms taken after the stomach had emptied showed retention of barium in this niche. The patient, however, is in excellent health and has absolutely no symptoms suggestive of an ulcer.

like pain, belching, indigestion, and persistence of preoperative complaints were reported at the time they presented themselves for postcholecystectomy x-ray studies. Careful scrutiny of the pyloric and duodenal regions, both fluoroscopically and roentgenologically, failed to reveal any evidence of the presence of spasticity, irritability, or ulcer formation in this group of patients.

CONCLUSIONS

1. Six of 75, or 8 per cent, of the patients in this series suffered from duodenal ulcer as well as chronic calculous cholecystitis.

2. The performance of cholecystectomy frequently leads to the subsequent x-ray findings of duodenal distortion or ulcer in patients who displayed normal x-ray findings preoperatively. This occurred in 8 patients, or 10.6 per cent, of this series.

3. In a patient who has been subjected to cholecystectomy, a deformed duodenal cap on roentgenographic examination does not necessarily signify the presence of an ulcer. In these cases, one should be guided in his diagnosis by the symptoms rather than by x-ray findings. The 8 patients in this series were symptom-free and in good health despite their abnormal x-ray findings.

4. In this series of cases, postcholecystectomy symptoms such as colic, belching, indigestion, and dyskinesia were not found to be associated with abnormal x-ray findings of the stomach and duodenum. Six of 75, or 8 per cent, of the patients suffered from moderate to severe postcholecystectomy symptoms but showed normal x-ray findings of the stomach and duodenum.

MULTIPLE PERITONEAL TRANSPLANTATION OF SPLENIC TISSUE FOLLOWING TRAUMATIC RUPTURE OF THE SPLEEN

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BY consulting numerous articles in the later years of the last century and early part of this one, it can be seen that there was a great deal of confusion about abdominal lymph nodes, hemolymph nodes, and accessory spleens. Vincent and Harrison in 1897 made the following statement:

"We believe that we have found gradual transitions from hemolymph glands on the one hand, to ordinary lymphatic glands, and on the other hand, to the structure of the spleen. So that no hard and fast line can be drawn marking off these structures from one another. A lymphatic gland has only to contain blood in part or the whole of its sinuses to constitute itself one of the varieties of hemolymph glands. In certain accessory spleens moreover, the splenic reticulum is so widened out as to approximate to a blood sinus of a hemolymph gland and the malpighian bodies are so diffuse as to resemble the lymphoid portions of the blood-lymph glands, so that spleen, hemolymph glands and ordinary lymphatic glands form almost a continuous series."

This opinion was confirmed by some investigators and not by others; some making the problem more complex by suggesting that there is a transition from fat to hemolymph nodes and back again to fat and others pointing to the confusion between hematomas and splenic fragments (the omentum in the case herein reported containing both). The literature from 1885 to 1915 or 1920 is quite voluminous, some of the articles appearing in zoological, anatomical, biological, and physiological journals. In recent years, in the discussions of accessory spleens and the transplantation of splenic tissues, there is less mention of hemolymph nodes. It seems to be rather categorically accepted that fragments of a ruptured or damaged spleen can be transplanted, though the occurrence is rare. One explanation given for the rarity is that it seems limited, for the most part, to children and because the number of patients with splenic ruptures who recover is not great. This reason may have had some validity when first used many years ago but does not seem to be very convincing now because there must be by this date many recorded laparotomies done in patients who have suffered ruptures of the spleen in their youth.

The spleen and the endometrium are the only structures that show this tendency to peritoneal transplantation.

Waugh has a very complete article on peritoneal transplants covering the subject well, in which he states that, up to the time of his paper in 1946, only 15 cases had been reported, making his the sixteenth and the only one in an adult. A survey of the literature since 1946 reveals only 2 other cases and the one herein reported, which seems to be the second adult in 19 patients.

When autotransplantation of the spleen or splenosis occurs it resembles, to some extent, the normal condition found in some invertebrates and higher fishes in which the spleen, as a single sizable organ, is absent and small bits of splenic tissue are found scattered in various parts of the abdomen. In the human, the spleen may be lobulated or the lobulations may go on to divisions into splenules. Accessory spleens are quite common and in doing splenic surgery there should always be a search for them. As many as 400 have been recorded in 1 patient. They can occur in the mesentery, omentum, on the gallbladder, near the stomach or kidney, or anywhere in the peritoneal cavity and have been found in the scrotum. Congenital absence of the spleen is occasionally noted, as is atrophy due to splenic

Fig. 1. The resected omentum with splenic implants showing.

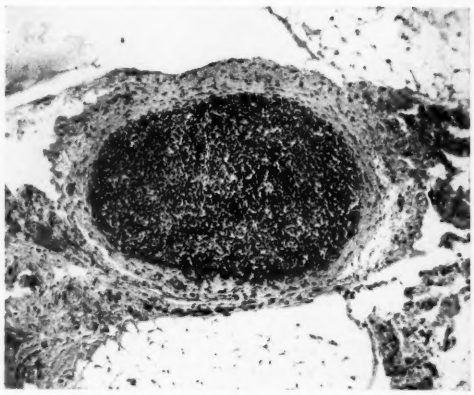

Fig. 2. The microscopic appearance of the splenic implants. Note the thick muscular capsule and the reticulum presenting a sinusoid system containing red blood cells. There is a small malpighian body containing an arteriole.

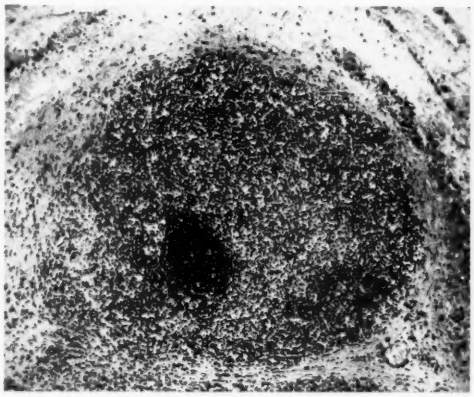

Fig. 3. Another microscopic implant with a more distinct malpighian body.

artery damage. Seventeen instances of absence have been reported.

Transplantation of splenic tissue is readily accomplished in experiments on animals. No cases are reported following splenectomy for diseased spleens, in which instance there must at times be contamination of the peritoneum with splenic tissue. It is suggested that only normal cells will grow. May it be that anlage of accessory spleens are present and scattered by trauma? In the photomicrograph it will be noticed that even the involuntary muscle of normal spleens is shown, possibly indicating anlage ancestry rather than splenic cells alone.

In the early part of this century there apparently was considerable interest in the effects of removal of the spleen and ligation of its vessels. It seems that in experiments on sheep and goats splenectomy gives rise to enlargement of abdominal lymph nodes, and there is discussion of possible formation of hemolymph nodes or splenic tissues. A summary in a paper by Warthin in 1916 is as follows:

"Splenectomy in dogs is not comparable in its effects upon the lymph nodes to the same operation in sheep and goats. In only 2 out of 24 dogs was any hyperplasia of the lymph nodes found, and no new-formation of hemolymph nodes or splenic tissues. . . . Ligation of the splenic veins seems to produce much more decided results after the lapse of 1 or 2 years following the operation. Three out of 8 dogs showed marked hyperplasia of the prevertebral nodes, and the 2 cases examined after longest intervals showed a new-formation of hemal nodes in the splenic region, the largest formed nodes resembling accessory spleens. These structures were not present at the time of the operation."

In neither splenosis nor aberrant spleens are there any characteristic blood changes diagnostic of their existence in an individual normal except for the removal of the spleen. The persistence of blood changes characteristic of certain conditions as hemolytic jaundice or some forms of purpura after splenectomy is strong evidence of splenic tissue remaining. (The increased fragility of red cells in hemolytic icterus remains after splenectomy even

when no other spleens are found at operation or autopsy.)

It may be asked how autotransplants can be distinguished from aberrant spleens. The answer seems to lie in the history of a damaged spleen and the absence of splenules at the time of the removal of the injured parent organ or at a later laparotomy, as in this case. This history with the known tendency to autotransplantation makes the evidence of splenosis presumptive. In the case herewith reported, there were organized hematomas in or attached to the omentum. This rather closely associated the splenules with trauma.

CASE REPORT

J. W., a 24 year old white male, was injured in an automobile accident February 23, 1951 and was taken into the Easton, Maryland, Hospital suffering with multiple fractures of the pelvis, severe contusion of the abdomen, and severe shock. During his stay at this hospital he received 11 pints of blood and on March 12, 1951 was transferred to Mercy Hospital, Baltimore, much improved, and he received conservative treatment only until April 3, when he began to have severe abdominal cramps, associated with vomiting and a sharp drop in blood pressure to 80/50. He was given another transfusion and adrenal cortical extract and operated upon later that day. A laparotomy showed old and fresh blood in the abdomen due to a ruptured spleen. The spleen was removed and for 3 days the convalescence was stormy, after which he slowly improved and was discharged May 4, 1951 with a red blood count of 3.94 and hemoglobin 11.7, the platelets being 553,000.

On May 26, 1951 he was readmitted because of pain in the abdomen and nausea, with a white blood count of 11,400. The diagnosis was partial intestinal obstruction, and operation showed a band leading from under the mesentery across the distal ileum with dilated proximal intestine. The band was released and a normal appendix removed. He was discharged June 4, 1951.

On December 31, 1951 he was readmitted because of abdominal pains and nausea but, after x-ray and other studies, operation was not advised and he was released on January 9, 1952.

On January 26, 1952 he was readmitted with pain in the right lower and left upper quadrants and again presented a picture of partial intestinal obstruction. Until this time the patient had been attended and operated upon by Dr. Joseph J. Jerardi. At the time of this admission Dr. Jerardi was ill, and the patient was referred to the writer, who operated upon him January 28, 1952. Abdominal adhesions were released and a band across the ileum similar to the one previously severed was again found and removed. Because of the pain in the left upper quadrant, this region was explored and, after adhesions of the omentum to the parietal wall were released, the omentum was found to be studded with splenic transplants to the number of 10 to 20, varying in size from a pinhead to 2 centimeters in diameter. The separation of the omentum from the parietal peritoneum resulted in so many perforations that it was thought safer to remove it, the patient being a thin individual and the omentum quite veil-like. This was done and the postoperative course was uneventful. The patient was discharged February 5, 1952.

SUMMARY

A case is presented as one of multiple peritoneal transplantation of splenic tissue following traumatic rupture of the spleen. There is brief discussion of some of the confusing aspects of clinical and experimental observations in this type of case.

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THE USE OF A LATISSIMUS DORSI PEDICLE FLAP GRAFT IN RADICAL MASTECTOMY

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THERE are certain cases of carcinoma of the breast which present difficult problems of reconstruction if the presently accepted tenets of good cancer surgery are observed. This is particularly true of the carcinoma which lies high and lateral to the nipple in the axillary tail of the breast. Most surgeons who propose to cure breast cancer agree that a margin of skin measuring at least 5 centimeters on all sides of the primary gross cancer must be resected with the block of tissue in order to be reasonably safe. If an area of skin measuring at least 10 centimeters in diameter (and more is usually necessary considering the area of the gross tumor) is resected from the region of the axilla and upper arm, then some satisfactory method of covering the neurovascular structures of the axilla must be employed. Pedicle skin flaps often may be mobilized to cover these structures with success; however, if a slough of skin develops over this area, then severe neuropathic or hemorrhagic sequelae may ensue. Healing at best in this region is not good after radical mastectomy. If a muscle flap is used under a skin flap or graft there is not only more chance that the skin will take but there is a double assurance that the neurovascular structures will be covered.

An analogous situation was met in the inguinal region by Baronofsky, who reported the use of a pedicle flap of sartorius muscle to cover the neurovascular structures following radical inguinal dissection. Healing was enhanced by this simple maneuver in Baronofsky's cases as well as in 3 similar cases done by one of us (H. G. M., Jr.). The advantage, of course, is due to the introduction of new blood supply to the region as well as to decreasing the chances of injury to the nerves and vessels from a slough. In such a situation an Ollier-Thiersch graft may be applied to the surface of the mobilized muscle with excellent expectation of growth.

In 1937 Rienhoff reported the use of a pedicle flap of latissimus dorsi muscle as a muscle bridge from arm to thorax in order to diminish the extent of postmastectomy arm lymphedema. He divided the latissimus and sutured it to the chest wall and residual cuff of pectoralis major. He stated that in 4 cases so treated there was no arm swelling or functional impairment of the arm.

The authors have used a muscle pedicle flap of latissimus dorsi in 2 cases with high lateral breast carcinomas. The primary purpose was to provide a safe means of protecting the axillary structures from the danger of poor healing and slough. It will be seen that in both of our cases healing was satisfactory, but that the pedicle graft did not prevent lymphedema.

TECHNIQUE

The technique for radical mastectomy is carried out in the orthodox manner by removal of the pectoralis major and pectoralis minor muscles in continuity with the breast, excised skin, and fatty and lymphatic tissue of the axilla. The latissimus dorsi muscle is dissected somewhat more extensively from the skin and underlying chest wall than is usually done. Figure 1 shows the dissection after the breast has been removed. The proposed line of incision of the latissimus dorsi is indicated. The muscle is partially divided distal to the entrance of the main portion of the innervation. The mobilized superior portion of the muscle is now reflected superiorly to cover the neurovascular structures of the axilla. It is sutured to the cuff of pectoralis major on the clavicle, to the chest wall and to the coracobrachialis muscle. As seen in Figure 2, the pedicle flap of muscle provides

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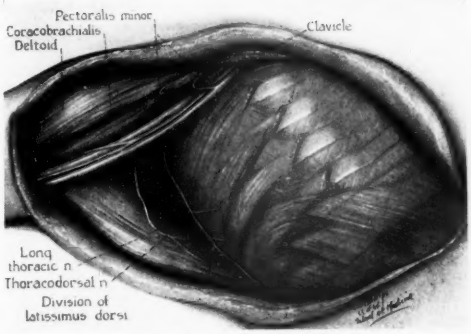

Fig. 1. Drawing of dissection with indication of proposed line of incision of latissimus dorsi muscle.

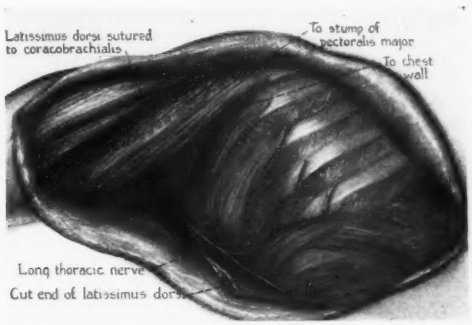
Latissimus dorsi sutured to coracobrachialis
To stump of pectoralis major
To chest wall
Long thoracic nerve
Cut end of latissimus dorsi

Fig. 2. Drawing demonstrating muscle graft sutured in to place.

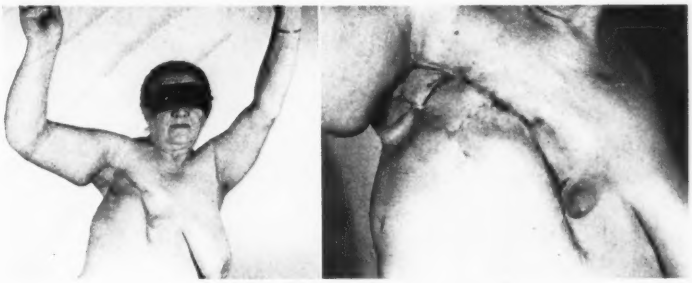

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Fig. 3. Case 1. Photographs taken 3¼ months postoperatively. a, Distant view with arm in abduction; b, close-up of same.

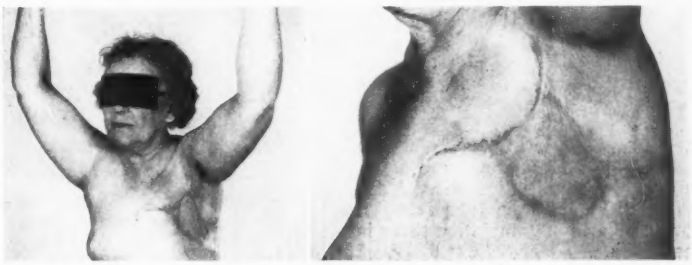

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Fig. 4. Case 2. Photographs taken 6¼ months postoperatively. a, Distant view with arm in abduction; b, close-up of same.

a complete and satisfactory protection for the axillary structures. Any residual skin defect may be covered with a split thickness skin graft with good expectation of a primary take either on the muscle flap or on the chest wall as the occasion demands.

CASE REPORTS

CASE 1. V. P., No. 292208, a 61 year old white female, entered the hospital with a 6 weeks' history of a mass in the right breast. The patient was obese. There was a hard mass measuring 6 by 4 centimeters in the upper outer quadrant of the right breast. The mass was attached to the underlying muscle fascia

but not to the skin. There were no palpable axillary lymph nodes or other evidence of distant metastases.

On May 13, 1952, the mass was biopsied, and a pathologic report of mucinous carcinoma of the breast was rendered.

On May 19, 1952, a right radical mastectomy was performed. At the conclusion of the dissection no skin was available for covering the axillary structures. The latissimus muscle flap was mobilized as described previously, and a split thickness skin graft was applied to the graft. Healing was prompt, but, because the patient lived out of town, she was kept in the hospital until June 16, 1952, for the purpose of aspirating fluid from beneath the skin flap of the lower portion of the operative field.

She was seen again on September 3, 1952, as an outpatient, at which time the photographs shown in Figure 3 were taken. There was some limitation of abduction by two webs of scar along the lines of healing of the graft. She can comb her hair, milk a cow, and drive an auto. She complained of mild tightness of the axilla when the arm was dependent. She had no paresthesias. Extremity circumference measurements on September 3, 1952 were: right forearm, 31 centimeters; left forearm, 28 centimeters; right arm, 30 centimeters; left arm, 32 centimeters.

CASE 2. L. C., No. 292350, a 68 year old white female, was admitted with a 6 weeks' history of a mass in the left breast. Physical examination revealed an irregular, poorly defined 2 by 3 centimeter nodule in the upper, outer quadrant of the left breast. There was slight skin dimpling over the lesion. No enlarged axillary nodes were noted. There was no evidence of distant metastases.

On May 20, 1952, a biopsy of the mass showed scirrhous carcinoma of the left breast.

On May 26, 1952, a radical mastectomy was performed. Again the skin available for covering the axillary structures was scanty and a latissimus muscle graft was applied. A split thickness skin graft was applied over the lower margin of the muscle flap. Her postoperative course was complicated by a 50 per cent pneumothorax in the left chest. She responded readily to one aspiration of the chest, and the lung remained expanded. There was a thin strip of skin slough along the graft margin, and a few pinch grafts were applied to fill in this defect. She was discharged from the hospital on June 23, 1952, healed except for a tiny area of granulation tissue in the region of the slough.

On December 4, 1952 (6¼ months postoperatively) she was seen as an outpatient and the photographs shown in Figure 4 were taken. There was no evidence of carcinoma at that time. There was slight limitation of abduction, but otherwise the function of the arm was good. Healing was complete. Extremity circumference measurements on that date were: right forearm, 25 centimeters; left forearm, 30.5 centimeters; right arm, 29 centimeters; left arm, 32.5 centimeters.

DISCUSSION

The use of a latissimus muscle flap to cover the vessels and nerves of the axilla consumes very little additional operative time and this step in the operation is quite simple to perform. In certain instances, particularly when the lesion lies high and lateral, this method provides a satisfactory covering and protection for the axillary structures.

If it develops that this graft promotes better lymph drainage from the arm, as has been suggested by Rienhoff, then it perhaps would be advantageous to perform this maneuver routinely. Early followup in our 2 cases, however, does not support Rienhoff's contention.

SUMMARY

A technique for utilizing the latissimus dorsi muscle as a satisfactory covering for the axillary structures following radical mastectomy for high and lateral breast carcinomas is described and illustrated.

Two cases in which this technique was used are presented, the early follow-up indicating that this maneuver does not prevent postmastectomy arm swelling, but that it does provide satisfactory protection of the neurovascular structures of the axilla.

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PARALYSIS OF THE MUSCLES OF THE CHIN

Surgical Treatment

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PARESIS or paralysis of the depressor muscles of the lower lip (quadratus labii inferioris and mentalis) is relatively frequent. A simple and effective surgical procedure is proposed for its correction.

The depressor muscles of the lower lip are innervated by the facial nerve. According to the classical anatomical description by Spalteholz, the nerve divides into two main trunks, temporofacial and cervicofacial, at a short distance from the stylomastoid foramen. The first trunk is distributed in the upper half of the face and forehead, but the second runs downward, lateral to the posterior border of the ascending ramus of the mandible. The ramus cervicalis, at some part of its course, divides into a series of branches which can be classified into three groups: (1) rami buccales, supplying muscles of the lower half of the face; (2) ramus marginalis mandibulae, distributed among the muscles quadratus labii inferioris and mentalis; and (c) ramus colli, descending toward the neck and ending in the platysma.

For the purpose of our procedure we must deal with the chin branches. The surgical anatomy is important, both from the viewpoint of corrective treatment and for the prevention of paralysis, since variations have been described in the literature.

Bertola described a lower trunk divided into two rami. Both are directed forward. The first ramus leaves the anterior border of the parotid at the angle of the mandible parallel to the horizontal ramus and 1 centimeter above its lower border, ending at the labial commissure. The second or true marginalis mandibulae also leaves the anterior border of the parotid and travels forward, but against the lower border of the mandible or up to 1 centimeter below it. At the middle of the lower border this nerve crosses it and divides into fine branches for the quadratus and mentalis muscles. This ramus has also been well studied by Poggiolini (cited by Stoppato) who described three variations: (1) the ramus passes a little above the inferior border of the mandible and may be mistaken for buccal branches; (2) it reaches the border at the suprahyoid region; (3) it forms an arc in the same region.

It is easy to injure the ramus marginalis during surgery in the submaxillary region and around the angle of the mandible when variations are like those described in (2) and (3). To prevent it, Poggiolini suggests incisions outside a quadrangle of safety which, in the adult with the head turned to the opposite side, is limited above by the inferior border of the mandible, below at 2.5 centimeters under this border, behind by the anterior border of the sternomastoid muscle, and in front by a vertical line running between the middle and anterior third of the mandible (Fig. 1). The nerve lies in the supra-aponeurotic layer. Flaps of this region should include the platysma and the fascia superficialis, to avoid damage of the nerve. Adson and Ott and Sistrunk have advocated locating and tracing this ramus, as a guide to reach the facial nerve trunk in parotidectomy with preservation of the nerve. However, since this ramus is not always easy to find, buccal branches have been preferred (7). The ramus marginalis, which is thin and fragile, is originally surrounded by parotid tissue. Then it passes through celluloadipose tissue behind the angle of the mandible, where its mobility makes dissection difficult, especially in obese subjects and women. The middle and anterior thirds of this nerve rapidly reduce in caliber when it divides to supply the muscle fibers.

PARALYSIS OF THE RAMUS MARGINALIS MANDIBULAE

The injuries of the nerve with which we are here concerned are of frequent occurrence, but

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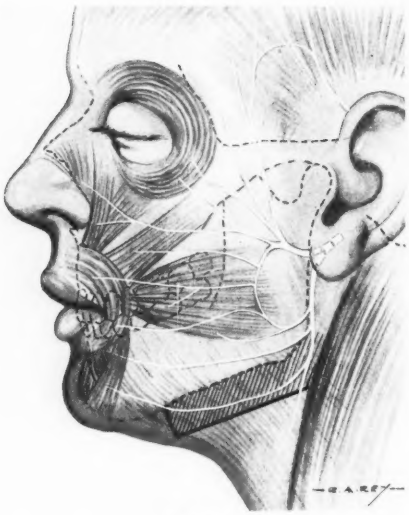

Fig. 1.

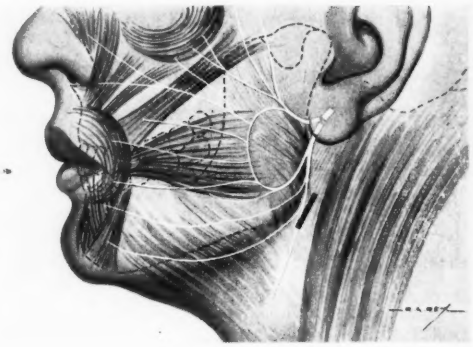

Fig. 2.

Fig. 3.

Fig. 1. Poggiolini's quadrangle of safety. Incisions within the limits of this quadrangle might damage the ramus marginalis mandibulae.

Fig. 2. Proposed incision for investigation of the ramus marginalis.

Fig. 3. Response of the muscles of the lip to the electrical stimulation of the ramus marginalis mandibulae.

because they cause little discomfort and their symptoms are seldom recognized, diagnosis is rarely precise. In our cases the most frequent cause was section of the nerve during incision and drainage for abscess of the angle of the mandible, especially in children. Other surgery included submaxillary incisions within the quadrangle of Poggiolini and supra-aponeurotic dissection of flaps in the region (radical neck dissection, and submaxillary gland removal). We have also observed obstetric, poliomyelitic, and cryptogenetic cases. The paralysis may remain as the only sequela of spontaneous regression of facial palsy, especially of poliomyelitic origin.

This paralysis in the face differs from others in that, while relaxed, the patient appears normal, but when the patient commences to talk, especially on pronouncing an "f", the asymmetry becomes immediately evident with contraction toward the unaffected side. The deviation increases on opening the mouth, and a depression toward the normal side is seen in the circle of the oral aperture. Pseudo-compensatory contracture is also observed, and the picture may be complicated with a series of twitches and movements which markedly distort the face.

SURGICAL TREATMENT

Suture of such a thin nerve, in a difficult surgical environment, is impossible except in selected cases. Usually these patients come for treatment with paralysis of long standing. Fascia suspension and muscle transplant operations are not successful in this form of partial paralysis. So far no other effective method of treatment has been proposed.

Some years ago R. Finochietto suggested section of the nerve of the opposite side to the paralysis. Thus, the paralyzation of the corresponding muscles will bring equilibrium in

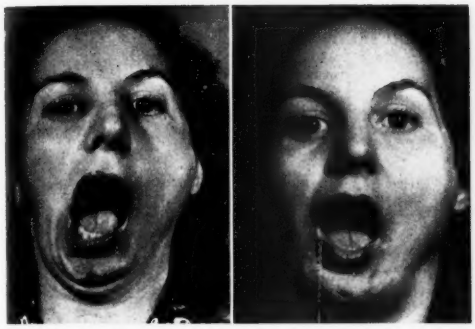

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Fig. 4.

a b

Fig. 6.

a b

Fig. 5.

Fig. 4. Preoperative and postoperative aspect of a patient with paralysis of the ramus marginalis of surgical origin (bone graft to the left side of the face).

Fig. 5. Preoperative and postoperative aspect of a patient with paralysis of the marginalis branch (left side) of obstetrical origin.

Fig. 6. Preoperative and postoperative aspect of a patient with paralysis of the marginalis branch (left side) of poliomyelitic origin.

muscle function and symmetry in facial expression. Criticism of this treatment was: the necessity of a comparatively long incision and the disastrous possibility of cutting the buccal branches due to anatomic variations.

We wish to describe a procedure for neurectomy of the ramus marginalis mandibulae, which we consider will eliminate these objections.

It is important, before proceeding with surgery, to ensure the result. To this end, we inject a few cubic centimeters of 2 per cent novocain near the angle of the mandible to block the nerve. If the reaction is satisfactory, operation is indicated.

A cortical stimulator, with bipolar electrode, should be added to the usual plastic surgery set. The whole of the face should be prepared and left uncovered in order that the side of operation may be compared with the other side. Local anesthesia is contraindicated. We use light sodium pentothal so that analgesia can be obtained but peripheral nerve excitability preserved. A minimal incision is made about 1 centimeter behind the angle of the mandible. The subcutaneous tissue is bluntly dissected and the layer of the nerve rapidly reached (Fig. 2). The nerve is located and traced. This is easy with the electrical stimulator gauged between 1 and 2 volts. It will take but a few seconds to find it, dissect it, and suspend it with a small hook. The stimulator will also determine exactly the group of muscles supplied by the suspended nerve, and so avoid damage to the buccal branches (Fig. 3). Neurectomy is performed, a few millimeters of the nerve being removed to prevent regeneration.

RESULTS

So far we have operated upon 7 patients. Results have been uniformly good. The patients complain of no inconvenience due to the moderate reduction in size of the oral aperture, from paralysis of the lower lip depressors. Speech is not altered. The scar is minimal. Up to the present time we have observed no recurrence of the deformity (Figs. 4, 5, and 6).

SUMMARY

Treatment is proposed for unilateral paralysis of the depressor muscles of the lower lip by excision of a portion of the ramus marginalis mandibulae of the facial nerve of the unaffected side. This is performed through a minimal incision and controlled by electrical investigation.

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EOSINOPHILIC GRANULOMA OF THE VULVA

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THE disease entity which is characterized by the histologic lesion referred to as eosinophilic granuloma has such a varied clinical picture, both from the standpoint of organs involved and duration of the disease, that it has not been until recent times that an understanding of the process has evolved. Originally, eosinophilic granuloma of skin was considered a separate disease from eosinophilic granuloma of bone, until recently when Lever and others have noted a few cases in which both tissues were involved. Eosinophilic granuloma of bone was also separated from Hand-Schüller-Christian disease. However, Green and Farber called attention to the histologic and clinical similarity between these two conditions and further concluded that such an apparently remote condition as Letterer-Siwe disease should also be considered as merely another expression of this one basic disease process.

Recently, 3 cases have been encountered, in which a combination of some of these entities was found and which seem to be links in the chain binding them into one category. They are presented because of the peculiarity and distinctiveness of the skin involvement in the vulvar region, because of the advanced ages of the patients and long duration of clinical findings, and because they appear to us to be examples of Hand-Schüller-Christian disease with the histologic pattern of eosinophilic granuloma rather than that of lipogranulomatosis.

CASE REPORTS

CASE 1. D. M., a white unmarried female, entered the Lahey Clinic in 1937 at the age of 42 complaining of fatigue and attacks of suffocation for the past 2 years. She had noted exertional dyspnea and tightness in the chest over the same period of time. She also complained of canker sores in the mouth for 1 month and headache, particularly in the frontal region, for the past several years. Physical examination at this time revealed an obese patient with Heberden's nodes of the finger joints. Her hemoglobin was 89 per cent and the red blood cell count was 4.13 million.

She entered the hospital again in 1944 complaining of a skin eruption for the past 4 months. The eruption began on the neck and on the ventral aspect of the right wrist. It consisted of tiny red blisters which were associated with pruritus. These spread up the ventral aspect of the arm and then appeared on the inner surfaces of the thighs. At the time of examination these lesions were found on the abdomen and consisted essentially of vesicles which tended to coalesce and then become blood crusted papules. Some of the lesions were annular in arrangement with scarred umbilicated craters. Her hemoglobin was 97 per cent with a red blood count of 4.6 million and a white blood cell count of 7,300.

The patient's chief complaint upon admission in April, 1945 was uncontrollable thirst associated with frequency which had been present for the past 6 months. She drank 3 quarts of water during the night and an increased quantity during the day. The urine was sugar free. She was placed on a maintenance dose of 1 minim of pitressin in oil every 60 hours which relieved her thirst and polyuria. Roentgenograms of the skull taken at that time were negative.

In 1946 the patient entered the hospital for a routine checkup and at this time hemoglobin was 13.6 grams with a red blood cell count of 4.6 million. The red blood cells showed a slight variation in size and shape.

Upon admission in 1948 she complained of faintness and dizziness which had a sudden onset and was associated with falling to the ground on one or two occasions. Physical examination revealed lichenified plaques on her right ankle. Her blood pressure at this juncture was 150/90 and a blood film revealed hypochromia and microcytosis of the red blood cells.

In 1952 she was admitted to the Free Hospital for Women with a history of itching and swelling of the labia minora of the vulva for the past year and 4 months. There was intense pain on micturition or while taking a bath which often became so intense that it was painful for her to sit in a chair. Three months prior to admission she noted an opening on the right labium minus from which a watery bloody fluid exuded. She also complained of weak-

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Fig. 1. Case 1. Gross photograph of vulva. The clitoris is eroded and ulcerated. The labia minora are elevated and firm, yellow-brown in color, and symmetrically involved.

ness, loss of appetite, cramps in the muscles of the lower legs and feet, and difficulty in seeing.

Her menopause had occurred at the age of 51 in 1946. Menses had started at the age of 12, each period lasting 5 to 6 days and occurring every 28 to 30 days. Physical examination revealed a well nourished, normally developed white female with no evidence of systemic disease. On the top of her head, beneath the scalp was a 5 centimeter movable mass which she had noticed for the past 3 months. A similar subcutaneous nodule was present in the right occipital region. Neither of these masses was tender or painful. However, there was a sensitive painful spot in the left temporal region.

Pelvic examination revealed a 1 centimeter ulcerated area to the right of the clitoris which was indurated and had tender raised red edges (Fig. 1). The labia minora were raised and swollen and had a peculiar yellow-orange color. Roentgenograms of the skull, femoral, and iliac bones revealed irregular punched out radiolucent areas. A moderate amount of sclerotic bone was present in the vicinity of the lesion in the iliac bones (Figs. 2 and 3). The hemoglobin was 8.8 grams per 100 cubic centimeters while the red blood cell count was 4.5 million. Blood films revealed a hypochromic microcytic anemia with numerous polychromatophils. The white blood cell count was 14,350 with 77 per cent neutrophils, 12 per cent lymphocytes, 8 per cent monocytes, 2 per cent basophils, and 1 per cent eosinophils. Blood sugar determinations had always been within normal limits and no sugar had ever been demonstrated in the urine. Biopsies were taken of the vulvar ulcer and one of the masses in the scalp on June 6, 1952. Seven days later the clitoris and labia minora were excised. The patient recovered uneventfully and went home 7 days later.

Pathology. FHW-S-52-2476. Grossly the specimen consisted of a triangular mass of skin and subcutaneous tissue. The labia minora were elevated and nodular with knob-like projections from the surfaces. The tissue was amber colored. To the left and just above the junction of the labia minora was a crater 1 centimeter in diameter with a necrotic center and raised edges. The tan necrotic tissue extended to a depth of 1 centimeter beneath the surface.

Microscopically, the connective tissue of the labia minora was infiltrated with a variety of cells. The major histologic feature was the presence of large numbers of histiocytes with pink granular cytoplasm and nuclei of varying shapes and sizes. Some were round, others reniform, and still others appeared folded and multilobulated. Eosinophils were present either singly scattered among the histiocytes or grouped together in small clusters. Numerous polymorphonuclear neutrophils were present and distributed in a similar fashion. Occasional lymphocytes and plasma cells were also scattered diffusely through the tissue. This infiltrate extended to the ulcerated surface and in some areas to the epidermis, but for the most part was separated from the epidermis by a thin layer of connective tissue. A few necrotic areas were present and these contained evidence of old hemorrhage in the form of hemosiderin filled macrophages, a few of which had fused to form multinucleated giant cells without hemosiderin were also seen in other areas and many of these had phagocytosed cells in their cytoplasm (Fig. 5). Two large lymphoid follicles with active germinal centers were buried in the midst of this sea of histiocytes and eosinophils (Fig. 6).

Two findings of particular interest were: (1) a marked inflammation of the walls of several small vessels (apparently arterioles or small arteries) (Fig. 7), and (2) the presence of numerous histiocytes and eosinophils in the lumens of endothelial lined spaces (apparently veins or venules). The latter were widely separated and not held together as compactly as the histiocytes and eosinophils in the tissue around them (Figs. 7 and 8). Reticulum stains revealed numerous reticulum fibrils extending in between individual cells (Fig. 9).

Biopsies of the skull lesions revealed an identical histologic picture.

Follow up. Further blood studies done 2 months after her discharge from the hospital on August 20, 1952 revealed a hemoglobin of 8.6 grams, a red blood cell count of 3.14 million, a hematocrit of 31, a white blood cell count of 10,000 with 53 per cent neutrophils, 28 per cent lymphocytes, 5 per cent monocytes, 4 per cent band forms, and 10 per cent eosinophils. A blood film contained numerous polychromatophilic red cells, target cells, and hypochromic microcytes.

CASE 2. J. M. H., a 29 year old married female, was first admitted to the Peter Bent Brigham Hos-

Fig. 2. Case 1. Roentgenogram of the skull taken in 1952, showing irregular punched out radiolucent areas. The sella turcica is not enlarged.

Fig. 3. Case 1. X-ray film of pelvis taken in 1952 showing radiolucent areas in right femur and both iliac bones. There are also areas of increased density in left iliac bone.

pital in February 1951 with a chief complaint of severe headaches. At the age of 19 she had a sudden onset of polyuria and polydipsia. One week later after the urine failed to show evidence of diabetes mellitus her physician made the diagnosis of diabetes insipidus, and treated her with 1 cubic centimeter of pituitrin every 12 hours. This controlled the diabetes insipidus but was accompanied by blanching of the skin, muscular contractions, and nausea. At the age of 20, pitressin tannate, 1 cubic centimeter every 2 to 4 days, was started and has controlled the diuresis to the present time. X-ray examination of the skull revealed no destruction of the sella turcica. Her basal metabolic rate was low and thyroid extract (1 grain a day) was prescribed. Menses had been regular until pituitrin medication, when they ceased for 1 year. Subsequently they became infrequent and irregular in length and duration. She has never been pregnant. Soon after marriage at the age of 22, painful, punched out ulcers with hard white centers appeared on the vulva. Gradually they became confluent. Serological tests were negative and novarsan treatment ineffective. Silver nitrate application brought transient relief. At the age of 25 similar lesions appeared on the gingiva and hard palate. One year later débridement of the vulvar lesion was performed and the diagnosis of nonspecific granuloma was made. X-ray treatment produced a remission. The ulcers of the palate were biopsied 6 months later and the diagnosis of Hodgkin's disease was suggested.

At the age of 27 the hard palate received a total of 3,500 roentgens which caused a complete remission of the lesions. In that same year new lesions appeared on the gingiva and on the vulva. Biopsies of these lesions were still considered Hodgkin's disease. Irradiation again was followed by regression of the ulcers. Cultures grew Streptococcus faecalis and diphtheroid bacilli. Aureomycin treatment caused a long lasting severe rash. X-ray examinations of the skull, facial bones, and chest were entirely negative.

At the age of 28 (September 1950) she had what appeared to be infectious hepatitis and lost 30 pounds. Subsequent studies revealed normal liver and gallbladder functions. Two months later small nodules appeared in the skin in the left submammary fold. The histology of these lesions in addition to the appearance of characteristic punched out areas in the skull and the history of diabetes insipidus led to the diagnosis of Hand-Schüller-Christian disease. The basal metabolic rate was −7 per cent. A fine diffuse pulmonary reticulation was seen on the x-ray films. The erythrocyte sedimentation rate was 61 millimeters per hour. The serum lipids were normal. After withdrawal of pitressin, the urine specific gravity stayed below 1.005. There was deafness in the left ear and roentgenograms showed partial destruction of the left petrous and mastoid bones. Diplopia was present and the left eye was slightly protuberant. Cortisone therapy was not beneficial.

In 1950 she entered the hospital because of increasingly severe headaches, hot flushes, and sweating. The positive findings at this time were, left exophthalmos; erythematous maculopapular rash in the left submammary skin; tender enlarged left axillary lymph nodes; tenderness on the left side of the skull; ulceration and discharge from the left ear; loss of hearing; several 3 to 5 millimeter sharply defined raised ulcers on the hard palate and right tonsillar pillar. Also there were several small tender vulvar ulcers with a malodorous discharge.

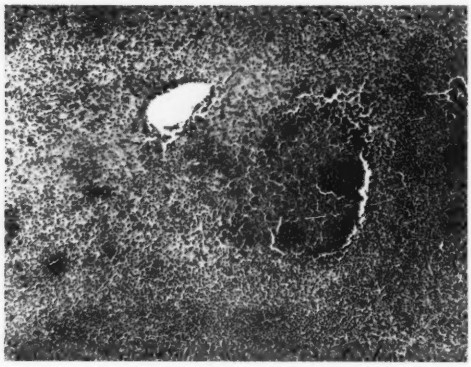

Fig. 4. Case 1. Photomicrograph of vulva showing an area of necrosis with scattered hemosiderin filled macrophages and giant cells. ×48.

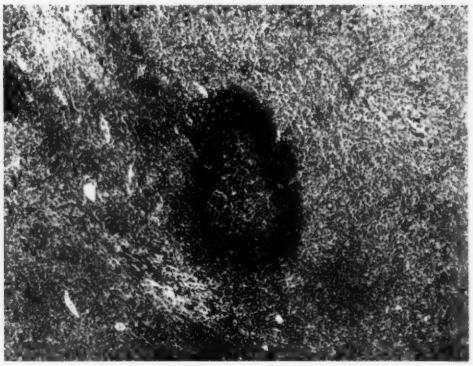

Fig. 6. Case 1. Photomicrograph of vulva showing lymphoid follicles with an active germinal center in the midst of the infiltrate. ×48.

A 4 hour epinephrine test and a 4 hour ACTH test resulted in a 75 per cent eosinophil drop. The urine was negative. Examination of the blood revealed a hematocrit of 41.5, a red blood cell count of 5.5 million, 5,700 white blood cells with 74 per cent neutrophils, 22 per cent lymphocytes, 1 per cent monocytes, and 3 per cent eosinophils. The blood urea nitrogen was 11 milligrams per cent, the total protein 5.9 grams per cent, the serum cholesterol was 120 milligrams per cent with 29 per cent free cholesterol. The erythrocyte sedimentation rate was 27 millimeters per hour. Roentgenogram of the chest revealed a diffuse reticulation that was most prominent in the right upper lobe. Three irregular 1.5 centimeter bony defects were found in the cranial vault including a large destructive area in the left petrous pyramid. The sella turcica was small and showed no evidence of destruction. In addition to 150 roentgens 4 times to the left petrous bone and 90 roentgens 5 times to the vulva and right chest, the patient received aminoamfol (folic acid antagonist) with improvement of the condition of the skin lesions.

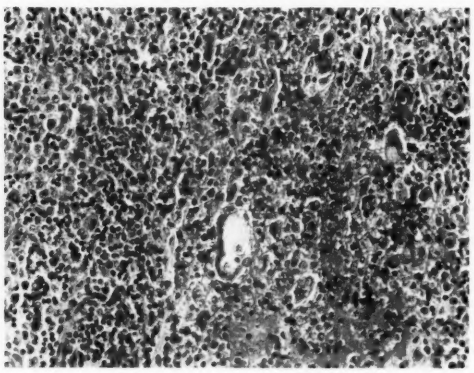

Fig. 5. Case 1. Photomicrograph of vulva showing a few multinucleated giant cells, one of which has a phagocytosed cell in its cytoplasm. ×188.

Five months later x-ray examination revealed larger skull defects and involvement of the first 2 sacral vertebrae. All her lower teeth had come out. Gingival ulcers reappeared as well as the skin mass in the submammary region. The right chest was irradiated again and in October of 1951 a therapy of 0.5 gram of para-aminosalicylic acid was given daily. The gingival ulcers disappeared.

In February 1952 the pulmonary findings had increased in severity and in May 1952 a dry hacking cough appeared with dyspnea on exertion.

In June 1952, nystagmus, a depression in the left parietal bone, and cough were prominent. The ulcers of the left breast and vulva had recurred. The left pupil was larger than the right. The white blood cell count was 6,200 with 48 per cent segmented forms, 10 per cent band forms, 23 per cent lymphocytes, 11 per cent monocytes and 8 per cent eosinophils. New bone formation was seen in the left mastoid area, but the x-ray findings in the roentgenogram of the chest suggested a progression of the pulmonary process. ACTH treatment (80 mgm. daily for 1 week, 40 mgm. daily for 2 weeks) had no noticeable effect on the respiratory function. Histoplasmosis tests were negative. The patient was discharged in an unchanged condition.

Pathology. Microscopic examination revealed an essentially similar inflammatory process in the mucosa of the roof of the mouth, the gingival mucosa and the submammary skin. The infiltrate was characterized by an irregular accumulation of large histiocytes with indented, irregular nuclei, and pink granular cytoplasm. Between the cells were scattered eosinophils, polymorphonuclear leucocytes and lymphocytes. Inflammatory cells were predomi-

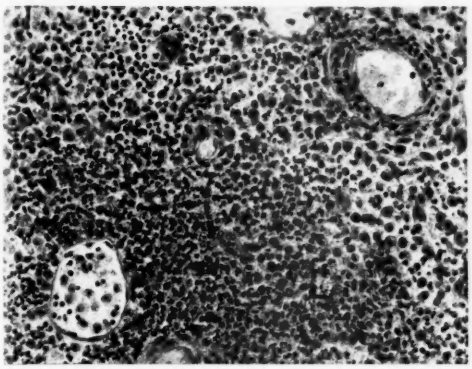

Fig. 7. Case 1. Photomicrograph of vulvar lesions showing inflammation of wall of small artery or arteriole and extension of histiocytes and eosinophils into the lumen of a vessel. ×188.

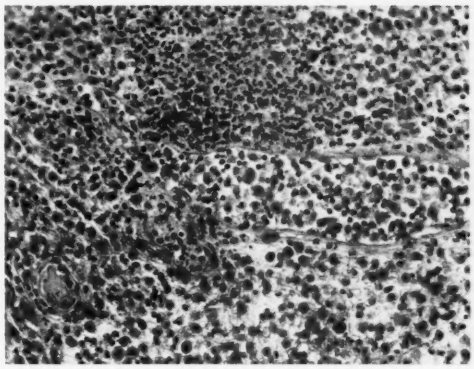

Fig. 8. Case 1. Photomicrograph of vulvar lesion showing extension of histiocytes, eosinophils, and lymphocytes into the lumen of an endothelial-lined space, either a vein or lymphatic vessel. ×188.

nantly in a perivascular distribution. No giant cells or lipophages were seen in any of these biopsies. The infiltrate lay immediately beneath the epithelium which was thickened with elongation of the rete pegs. A moderate amount of edema of the dermis was noted.

CASE 3. K. V., a 47 year old white married female, entered the Massachusetts Memorial Hospitals because of ulceration of the right groin. For 5 years prior to admission she suffered severe, recurrent pruritus of the perineum. One and a half years prior to admission red inflamed areas in the right groin began to ulcerate. She was treated with penicillin, "cream," and ultraviolet light with some improvement. The lesions were never tender.

System review revealed a history of frequency of urination, nocturia, and excessive thirst of 10 years' duration. There had been no loss of weight during this period. For 1½ years prior to admission she had noticed progressively increasing backache. Her menstrual periods have been irregular of late with passage of clots during menstruation. Physical examination revealed an obese woman in no acute distress. The blood pressure was 140/70, pulse 80 per minute and temperature 98.6 degrees F. Positive physical findings were limited to the perineum. In the left groin there was an erythematous, shiny, nonulcerated macular area involving most of the length of the inguinal fold. In the right groin there was a similar lesion with a superimposed longitudinal, superficial ulceration measuring 4.0 by 2.0 centimeters. The lesions appeared to be edematous, but not indurated.

Laboratory studies revealed the urine specific gravity to be 1.003. There was no evidence of albumin or sugar in the urine. Hematological studies revealed a hemoglobin of 14.6 grams per cent, hematocrit of 40.5 per cent, reticulocytes 7.5 per cent, white blood count 6,400 with 77 per cent polymorphonuclear leucocytes, 16 per cent lymphocytes, 6 per cent monocytes, and 1 per cent eosinophils. Blood chemical studies revealed the fasting blood sugar to be 116 milligrams per cent and the nonprotein nitrogen 33 milligrams. The blood Hinton test was negative.

A biopsy of the ulcerated area was performed and the lesions on both sides of the vulva were excised. Microscopic examination of the full thickness of the skin including some subcutaneous tissue revealed the corium to be largely replaced by a mass of large mononuclear cells. These had lobulated or indented, bean shaped nuclei and abundant, homogeneous, slightly eosinophilic cytoplasm. Multinucleated cells were occasionally seen. Mitoses were frequent, but none were atypical. Bizarre nuclei or tumor giant cells were not seen. Evidence of cytophago-

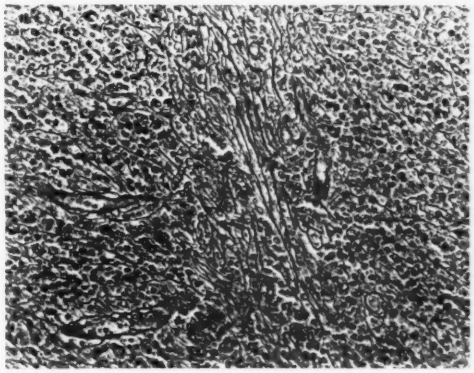

Fig. 9. Case 1. Reticulum stain of vulva. The reticulum fibrils are numerous and extend in between individual cells. ×141.

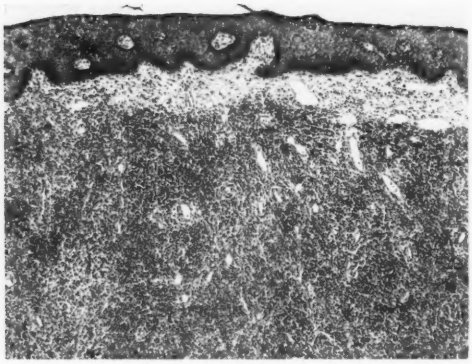

Fig. 10. Case 3. Photomicrograph of vulvar skin. In this region the infiltrate is separated from the epidermis by a thin layer of connective tissue. ×48.

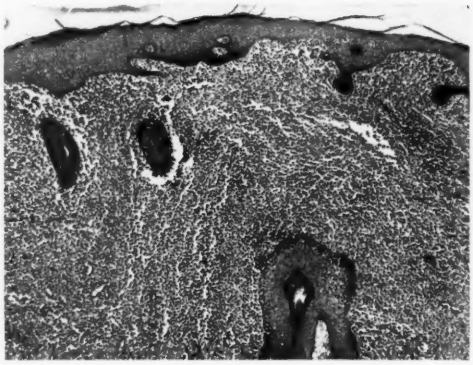

Fig. 11. Case 3. Vulvar skin. The infiltrate is shown to extend to the epidermis and surrounds skin appendages. ×48.

cytosis was inconspicuous, but a few large mononuclear cells contained granules of hemosiderin. The infiltrate encroached closely upon the skin appendages and epidermis and was prominent about the numerous small blood vessels. In several areas numerous bilobed, eosinophilic granulocytes were scattered amongst the large mononuclear cells. Near the ulcerated surface there were numerous segmented neutrophilic granulocytes. These cells were also seen in moderate numbers deep in the corium in sections taken from nonulcerated areas. At the edges of the mass of large mononuclear cells there were a number of lymphocytic aggregates and numerous plasma cells. In some areas the walls of small blood vessels were infiltrated with neutrophilic granulocytes and large mononuclear cells. These vessels showed moderate endothelial proliferation. There was no evidence of collagen deposition or fibroblastic proliferation either in or at the periphery of the infiltrate. Indeed, there was almost complete disappearance of collagen in the lesion. There was considerable edema in many areas as evidenced by pink staining granular material between the mononuclear cells. Foam cells were not seen and stains for fat revealed no evidence of lipid either intracellularly or extracellularly.

Following excision of the vulvar lesions the areas healed rapidly. However, it was noted that the patient's urinary output ranged from 5,325 cubic centimeters to 7,600 cubic centimeters per day during the hospital stay. She was discharged in good condition. Six months after discharge from the hospital there had been no recurrence of the skin lesions, but she continued to have polydypsia and polyuria. She refused further hospitalization for more complete studies.

DISCUSSION

Reports in the literature of eosinophilic granuloma involving the vulva are rare. Weidman has briefly described a patient with vulvar lesions that had been present for a year. They were cauterized and healed but subsequently the lesions reappeared. These were cauterized also, but the lesions recurred for the third time. Wile, in the discussion of a paper by Lewis and Cormia, has described vulvar involvement in an 8 months old child. The infant had ulcerating fungating lesions in the groin, on the tongue and buccal mucosa, and around the genitalia and axilla. Bony lesions were seen by roentgenogram and all these lesions disappeared with "mild irradiation." Curtis and Cawley have presented a case of involvement of the vulva in a 16 month old girl who at the age of 8 months developed an eruption on her scalp which consisted of red discrete coalescent papules which spread to involve the buttocks and genitalia. Painful erythematous eroded plaques were present in the mouth with macules and papules in the palate. The vulvar and perianal skin had denuded "weeping" surfaces. Roentgenograms revealed a destructive lesion in the right second rib, in the left ilium, and right mastoid. Lymph nodes were palpable in the cervical and inguinal regions. No mention was made of polydipsia or polyuria. X-ray therapy was followed by a gradual healing of all lesions.

A patient, described under the heading of Hand-Schüller-Christian disease by Dr. George Andrews in a discussion of a paper by Lane and Smith, had vulvar lesions. The pa-

tient was a 6 year old girl who had recurrent attacks of bullous eruptions of the scalp and vesicles on the vulva. She developed exophthalmos and biopsy of a mass on the skull was called Hand-Schüller-Christian disease. Miliary vesicles on the vulva in a day or two became small abscesses on the inner surface of the labia. A notable feature was the symmetrical distribution of the lesion.

EOSINOPHILIC GRANULOMA OF THE SKIN

In 1950 Lever and Leeper pointed out the confusion that prevailed in regard to eosinophilic granuloma of the skin. They proposed that the cutaneous lesions described under the term eosinophilic granuloma could be divided into three groups, namely: (1) cases associated with eosinophilic granuloma of bone, (2) cases characterized by torpid, asymptomatic, purplish patches on the face, and (3) a heterogeneous group of cases having nothing in common but a large percentage of eosinophils in a granulomatous infiltrate. Lever and Leeper eliminated the third group from their discussion because of the varied etiology and reserved the term eosinophilic granuloma for the first two groups.

According to these authors the reasons for separating the second from the first group were that the lesions: (1) occurred predominantly on the face, (2) were grossly different in that they were purple rather than yellow brown, (3) were covered by a normal appearing epidermis, (4) did not ulcerate, (5) were radioresistant rather than radiosensitive, (6) occurred in adults rather than children, and finally (7) were not associated with bone lesions. The histologic pattern was also slightly different.

These authors found 4 cases in the literature and added one of their own cases of eosinophilic granuloma of skin associated with bony lesions. All of these cases had their onset in infancy. Lipid material was absent from the lesions of all of these cases and no mention was made of diabetes insipidus.

The case which they presented was that of a 19 months old boy who at the age of 6 months was found to have a discharge from his external auditory canals. At 9 months a generalized skin eruption appeared, which

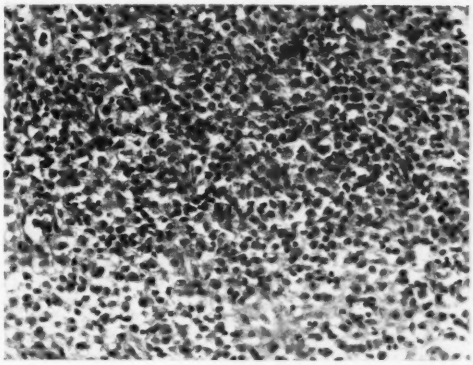

Fig. 12. Case 3. Eosinophilic granuloma of vulva. Nonlipid histiocytes and eosinophils predominate. ×188.

consisted of papules appearing first about the ears and spreading then to the scalp and trunk. The auditory canals were filled with granulation tissue. Cervical, occipital, axillary, and inguinal lymph nodes were enlarged. The tissue in the ears was curetted and the canals irradiated with remission of the masses. This was followed by the appearance of a mass on the scalp over the left ear which responded to x-ray therapy. The patient had an anemia with a hemoglobin of 9.4 grams. Histologically the tissue presented the appearance of eosinophilic granuloma.

Another case of great interest is that discussed by Montgomery in 1950. A 42 year old man entered with a chief complaint of pain and tenderness in the perianal region. At the age of 22 he had developed diabetes insipidus with polydipsia and polyuria which were controlled with daily injections of pitressin. At the age of 33 he had noted masses projecting from the palate, gums, and buccal mucosa. Over a period of a few months he lost all his lower teeth. Four years prior to admission he had developed a painful fissure and fistula in ano. Surgical excision of the fistula was followed by an abscess that failed to heal despite x-ray therapy. Histologically, the perianal tissue was eosinophilic granuloma.

EOSINOPHILIC GRANULOMA OF BONE

The original reports on this entity were presented in 1940 by Otani and Ehrlich and Lichtenstein and Jaffe.

It may be that Shairer's case described as osteomyelitis with eosinophilic reaction was actually the first case.

The cases included in these papers presented as solitary bone lesions and the patients were young and without other symptoms or signs. Farber in 1941 and Green and Farber in 1942 presented 10 patients with eosinophilic granuloma of bone, 4 of whom had solitary bone involvement and 6 of whom had multiple bony lesions. All these patients were under the age of 12 years, and 9 of the 10 were males. The x-ray appearance of these lesions was that of punched out round, oval, or irregular radiolucent areas. They developed rapidly and healed rapidly following irradiation. The distribution and appearance of the multiple lesions were identical with the picture seen in Hand-Schüller-Christian disease. Lesions were present predominantly in flat bones including the skull. Of the bones of the extremities, those closest to the trunk were most commonly involved. The distal ends of the tibia, fibula, radius, ulna, or bones of the hands and feet appeared unaffected.

Pain and/or swelling at the site of some of the bone lesions were the initial symptoms. Nine patients had a moderate anemia, 3 had headaches, none of the patients had diabetes insipidus, dwarfism, or central nervous system symptoms. Six of the 10 patients had a leucocytosis on admission which averaged 15,800 white blood counts. Following irradiation 1 patient developed an eosinophilia of 6 per cent.

In 1944 Jaffe and Lichtenstein presented 2 cases of eosinophilic granuloma of bone with involvement of several bones. In neither of these cases was the skull involved, nor was there any evidence of systemic disease. However, they pointed out the similarity of the x-ray appearance in these cases and in cases of Hand-Schüller-Christian disease.

They described 2 cases of spontaneous resolution of the lesions and their histologic studies suggested that this resolution occurred without the development of a stage of lipogranulomatosis which is according to Farber and others a later stage of the disease.

The etiology of this disease is not known. It does not appear to be of bacterial origin since attempts to isolate organisms, even after animal inoculations, have been unsuccessful. By the same token there is as yet no evidence that a virus might be the causal agent.

HAND-SCHÜLLER-CHRISTIAN DISEASE

Classically, Hand-Schüller-Christian disease is a clinical syndrome characterized by the triad of diabetes insipidus, defects in the skull, and exophthalmos. Cases described under this name have not always, however, exhibited all three symptoms. It is predominantly a disease of late childhood, although it occurs often in adults. Chester and Kugel found 33 of 50 cases reported in the literature in the first decade of life. Fifty per cent were children less than 5 years of age.

One third of the patients have skin involvement which may be a bronze pigmentation, a maculopustular rash, a hemorrhagic eruption, seborrhea-like lesions, or occasionally lipoid infiltrations of the eyelids. Gingivitis, with or without ulcers of the gums and loss of teeth, is found in 39 per cent of the cases. The spleen and liver may be enlarged and extremely rarely dwarfism will be a prominent feature clinically. Palpable fluctuant masses beneath the scalp or soft swellings of other bones are a frequent occurrence. Many cases exhibit a mild to severe anemia which progressively worsens as the disease advances. Hypercholesterolemia is not a prominent feature as was originally believed. Moderate eosinophilia is not an unusual occurrence and it may be so prominent in children as to be mistaken for myeloma or myeloblastoma.

Roentgenograms of the chest frequently show a diffuse mottled reticulation. Punched out, irregular, radiolucent areas in the skull or in many bones of the body are present.

At autopsy these patients present yellowish masses of the skin, mucous membranes, serous surfaces, tendon sheaths, or fascia. Yellow or grayish nodules are found in the liver, spleen, lungs, heart, lymph nodes, bone marrow, kidney, commonly in the meninges, and rarely in the central nervous system. The number of organs involved in any one case is variable.

The histology of these lesions at autopsy is basically that of an infiltrate of histiocytes.

Lane and Smith describe the microscopic picture as one of lipid laden foam cells, lymphocytes, plasma cells, leucocytes, and proliferating immature tissue. Foreign body giant cells, eosinophils, and areas of necrosis and hemorrhage may be present. Originally the disease was described as an infiltrate of lipid laden histiocytes and hence it was regarded as a lipoid storage disease. Most recent authors have followed the suggestion of Chester, Farber, and Letterer and have removed it from the category of lipoid storage diseases.

Of particular interest is the fact that, although basically similar, the histologic picture of lesions in one part of the body may vary from that in other regions, in small detail. Similarly the lesions vary somewhat from one case to another. Eosinophils may be prominent in some regions (and in some cases) and may be absent in others. Some lesions show abundant lipid in the cytoplasm of the histiocytes, while most of the lesions do not. In the latter area these histiocytes are described as having an acidophilic granular cytoplasm. Chester (2) and Lane and Smith are of the opinion that the foam cells represented the early form of the disease, while the granulomatous tissue was a late expression of the process. Ceelen, Gerstel, Farber, and Mallory on the other hand believed that the granulomatous form is the earliest expression of the disease, and that the foam cells appear in the later stages.

From autopsy material and from other cases it is quite clear that both histologic patterns may coexist in the same patient. Some organs such as liver, spleen, and lymph nodes seem to be less apt to develop the foam cells than others such as the bone and brain. It has not been satisfactorily demonstrated by sequential biopsies that all lesions go through the assumed evolution from histiocytic inflammation to lipoid granuloma. Mallory has stated that lesions biopsied early have shown the histology of eosinophilic granuloma and not that of lipoid granuloma. Also lipogranuloma is more apt to be associated with fibrosis and would, therefore, appear to be an older lesion from the purely histologic standpoint.

Except for the lung, the lesions are sensitive to x-ray therapy but frequently recur.

LETTERER-SIWE DISEASE

Letterer-Siwe disease appears mainly in infants and children below the age of 2 and rarely beyond the age of 4 years. It runs an acute or subacute course and is usually fatal in a few weeks or months.

Clinically the infants have a fever; enlargement of the spleen, liver and superficial lymph nodes; a cutaneous eruption, generally purpuric and most pronounced just before death; hypochromic anemia which becomes profound terminally; and one or more destructive lesions of bone, particularly in the skull bones. In addition, leucocytosis with secondary bacterial infection (otitis, mastoiditis, or inflammation of lymph nodes), mottling or "honeycombing" or emphysema of the lungs on x-ray examination, pleural effusion, ascites, and edema may also appear.

The histologic picture which has been described is essentially that of an infiltrate of histiocytes involving particularly the lymph nodes, tonsils, thymus, spleen, bone marrow, liver, lymphoid tissue of the gastrointestinal tract, lungs, dura, periosteum, connective tissue of the heart, pancreas, renal pelvis, pituitary, adrenal, and thyroid. Scattered among the histiocytes are lymphocytes, plasma cells, and occasionally eosinophils. Jaffe and Lichtenstein state that the bone lesions in Letterer-Siwe disease may be indistinguishable from eosinophilic granuloma of bone.

EVIDENCE OF THE CONCEPT OF ONE DISEASE

The most important evidence that eosinophilic granuloma of skin and bone, Hand-Schüller-Christian disease, and Letterer-Siwe disease are really different expressions of the same basic disease process is histologic. They all present the same histologic pattern except for certain occasional minor variations. Also, in general, each entity shows a tendency to involve certain specific tissues of the body; namely, bone, skin, lung, lymph nodes, spleen, and liver. This is probably an expression of the fact that it is a disease primarily involving the reticuloendothelial system.

In addition numerous examples of cases depicting transitions from one of these entities into another can be found in the literature. Eosinophilic granuloma of bone may progress

to Hand-Schüller-Christian disease. Engelbreth-Holm and associates have described 5 cases which started with solitary bone lesions that progressed to multiple bone involvement. Diabetes insipidus, disturbance of growth, and pulmonary changes appeared subsequently. Geschickter and Copeland have described 2 similar patients. One case began with a solitary fibular lesion and in 9 years skull defects of Hand-Schüller-Christian disease developed.

Eosinophilic granuloma may involve both skin and bone in the same patient. Lever and Leeper have collected 5 cases which illustrate this point, and our first case is an example.

Eosinophilic granuloma of bone may progress to Letterer-Siwe disease. Jaffe and Lichtenstein reported a case in 1944 of an infant with a bone lesion which was histologically an eosinophilic granuloma. One month subsequently the child developed a skin rash and died. Autopsy revealed the typical pathologic findings of Letterer-Siwe disease.

Letterer-Siwe disease may progress to Hand-Schüller-Christian disease. Merritt and Paige have described such a case in a 5 year old child who developed a fever, cutaneous rash, enlargement of the lymph nodes, spleen and liver, with diabetes insipidus, exophthalmos and defects in the skull. The illness lasted 2 years and terminated fatally. At autopsy the spleen, liver, and lymph nodes showed focal nodular collections of histiocytes such as are seen in Letterer-Siwe disease of the typical acute variety. However, in the skull bones, there were numerous lipophages in a meshwork of fibroblasts and collagen fibers.

The cases presented in this report also support the concept of one disease. In the first case the disease process began at the age of 49 with a diffuse skin rash similar to that described in patients with Letterer-Siwe disease. One year later diabetes insipidus appeared. No roentgenographic defects were present in the skull and the sella turcica was intact. Eight years later skull lesions typical of Hand-Schüller-Christian disease appeared in addition to the localized mass on the vulva. At this time the vulvar symptoms necessitated surgical excision. Histologically, the vulvar and skull masses were indistinguishable from eosinophilic granuloma of skin and bone.

In the second case the disease became manifest with the occurrence of diabetes insipidus at the age of 19 years. No skull defects were present in the x-ray films. At the age of 22 vulvar ulcers occurred. Two years later similar lesions with the histologic pattern of eosinophilic granuloma appeared on the hard palate. Repeated x-ray therapy to gingiva and vulva resulted in remission. At the age of 28 the skin in the submammary region was involved. Defects in the skull, identical with those seen in Hand-Schüller-Christian disease, and pulmonary infiltration with pulmonary symptoms as well as exophthalmos appeared at the age of 29, 10 years after the appearance of the initial symptom of diabetes insipidus.

Mallory has segregated the cases with this disease into three groups: (1) The disorder may manifest itself in infancy or very early childhood in an often rapidly fatal form in which the histiocytic lesions are widely distributed through the soft tissues (especially the lymphoid tissues) and the skeleton (so-called Letterer-Siwe disease, reticulosis, or nonlipid histiocytosis). (2) The disorder may appear in children or adults (even middle aged ones) in a chronic form, in which the histiocytic lesions, again not usually limited to the skeleton, tend to undergo collagenization and lipidization, and in which the prognosis is often still grave because of the likelihood of damage to the lungs and heart and to the brain and pituitary gland (Hand-Schüller-Christian disease or lipogranulomatosis). (3) The disorder may appear in children or young adults in a comparatively benign and much more localized form in which the lesions seem to occur only in the skeleton (and often only in a single bone), heal readily after simple curettage, even without supplementary therapy, and may indeed heal by resolution, even without any therapeutic intervention (eosinophilic granuloma of bone).

SUMMARY AND CONCLUSIONS

1. Three cases of eosinophilic granuloma involving the vulva are presented.

2. The vulvar lesions are often symmetrical and tend to be eczematous and exudative in children while in the adults they tend to be localized yellow brown tumors.

3. These cases provide additional evidence for the concept that eosinophilic granuloma of skin and bone, and Hand-Schüller-Christian disease are merely different expressions of the same basic disease process.

4. Eosinophilic granuloma is not confined to the younger age groups, and the disease process may be of many years' duration.

5. When the disease produces localized swellings in the skin, these masses tend to localize around body orifices, i.e., the mouth, external auditory canal, perianal region, and vulva.

6. The outcome in this disease is difficult to predict, but the disease tends to be shorter and more often fatal in infants and children and of longer duration when it appears in adults.

7. Therapy at present is inadequate to cure the disease in its more severe form, but palliative x-ray treatment or local excision yields temporary good results.

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THE URINARY EXCRETION OF CORTICOIDS AND 17-KETOSTEROIDS FOLLOWING MAJOR OPERATIONS

Correlation with Other Aspects of Metabolism

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THE physiology of surgical injury embraces a host of metabolic processes which in the aggregate permit the individual to survive. The purpose of this report is to present measurements of urinary steroid excretion in patients before and after operation, and to draw certain correlations between adrenocortical activity and the other metabolic activities which have been examined.

PROCEDURE AND METHODS

The patients studied were general surgical patients on the wards of the Hospital of the University of Pennsylvania. When the subject was selected for the project he was placed in a special cubicle or, later in the study, in the metabolic ward. Three of the patients had gastric resections, 1 had segmental colon resection, and 1 had a common bile duct exploration. Additional pertinent information appears in Table I. During the preoperative control period, which generally lasted from 3 to 7 days, 4 of the 5 patients were placed on a standard metabolic diet of natural foodstuffs consisting of 150 grams of protein and 2,100 calories. This dietary program was selected after several preliminary experiments had shown that it represented the maximum nitrogen and caloric intake which could be easily reached through intravenous alimentation during the first 3 postoperative days. Although larger intakes would perhaps have been desirable, this program had the advantage of permitting a constant intake. Moreover, the administration of the same intake to each patient, while varying fairly widely between individuals when expressed as calories and grams of nitrogen per kilogram of body weight, was not as disproportional when expressed on the basis of kilograms of "lean body mass." The intravenous alimentation in the immediate postoperative period was accomplished with amigen, 7.5 per cent alcohol, glucose, and saline solutions. It is recognized that parenteral feeding is inferior to the oral route. The total urinary nitrogen loss in 24 hours following a venoclysis of the protein hydrolysate of casein is greater than after the feeding of an equivalent amount of skim milk powder. However, it is very nearly possible to overcome a negative nitrogen balance with intravenous amino acids.

During the control period 24 hour collections of urine (and of feces, in the nitrogen balance studies) were made. Total eosinophil counts and the urinary excretion of corticoids (lipid soluble reducing substances), total neutral 17-ketosteroids, nitrogen, and preformed creatinine were measured. Urines were analyzed over a period of a few days to a few weeks for corticoids and 17-ketosteroids at intervals of from 1 to 13 weeks after collection. Urines were stored at 0 to 4 degrees C. and preserved with chloroform. Despite these precautions, it is considered probable that partial hydrolysis of the glucuronides of the corticoids may have occurred, so that absolute values are moderately higher than those obtained with analyses done on the day of collection. Never-

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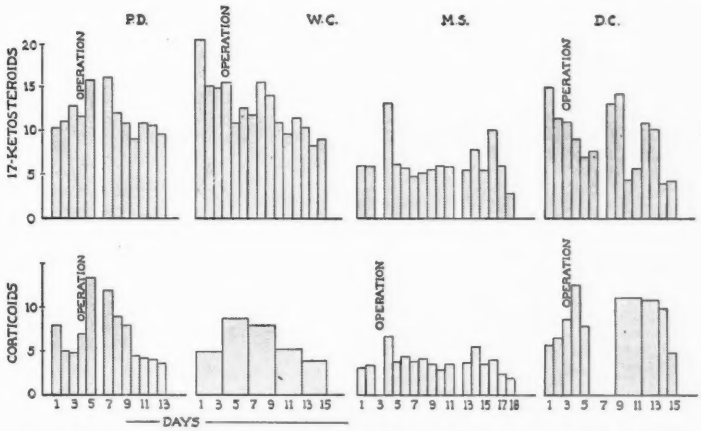

Fig. 1. Urinary excretion of corticoids and 17-ketosteroids before and after operation. All 4 patients exhibited a postoperative increase in the excretion of corticoids, but only 2 patients showed an increase in the excretion of 17-ketosteroids. The fifth patient, W. S., not charted here, also showed an increase in 17-ketosteroids.

theless, relative values for any one patient are believed not to be significantly changed by the delay in analysis. The concentrations of sweat sodium, chloride, and potassium were measured in the sweat collected in a large rubber glove by the simple expedient of giving the patient a cup of hot tea, placing hot water bottles at his feet, and submerging his hands and forearms in very warm water. A more rigidly controlled atmosphere would perhaps have been desirable, but a constant temperature room was not available for this study.

RESULTS

The results of the urinary steroid excretion studies in 5 patients are presented in Figures 1 to 7. The excretion of corticoids was increased following operation in the 4 patients so studied, the average duration of the increase being approximately 4 days. The excretion of 17-ketosteroids increased in only 3 of the 5 patients following operation. Thus the excretion of corticoids appears to be superior to the excretion of 17-ketosteroids as an index of adrenocortical response to stress (Fig. 1).

The correlation of the preoperative and postoperative total eosinophil counts with the urinary corticoid excretion in 4 patients is shown in Figure 2. There is a good inverse correlation between the 2 curves; moreover, in each instance both curves tend to return to the preoperative base line at approximately the same time. Therefore, the easily performed total eosinophil count would appear to reflect with some fidelity gross alterations in the level of adrenocortical activity.

In Figure 3 are illustrated the relationships which appear to exist between alterations in the level of urinary corticoid excretion and sweat electrolyte concentrations, as represented by the findings in patient W. C. following gastric resection. An increase in adrenocortical activity is associated with a prompt

TABLE I.

Patient	Age Sex	Diagnosis	Operation	Postoperative course
P. D. (Duf.)	53 M	Duodenal ulcer	Gastric resection	Very mild, maximal temperature 100° F. Perforated ulcer, closed 3 weeks earlier
W. C. (Col.)	62 M	Duodenal ulcer	Gastric resection	Moderately turbulent. Temperature 103° F. at close of operation; thereafter 99 to 100.8 degrees F. for 7 days
M. S. (Sew.)	65 F	Pancreatitis	Common duct exploration	Mild. Maximal temperature 100° F. "Weak and exhausted." Slow convalescence
W. S.	44 M	Duodenal ulcer	Gastric resection	Turbulent course. Sustained fever 17 days. Maximal temperature 102.6° F., etiology obscure
D. C. (Cun.)	51 M	Colon carcinoma	Segmental resection	Moderately turbulent. Maximal temperature 101.8° F., duration fever 8 days

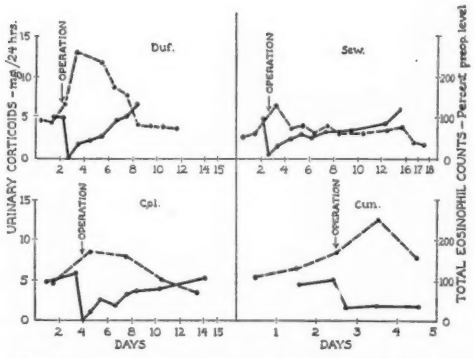

Fig. 2. Correlation of changes in urinary corticoid excretion with total eosinophil counts after surgery. In each patient there is a consistent inverse relationship between the 2 curves both of which tend to return to the preoperative levels at approximately the same time. Patient Cun. exhibited a prolonged increase in the excretion of corticoids and his total eosinophil count remained depressed for a correspondingly prolonged interval (Fig. 6).

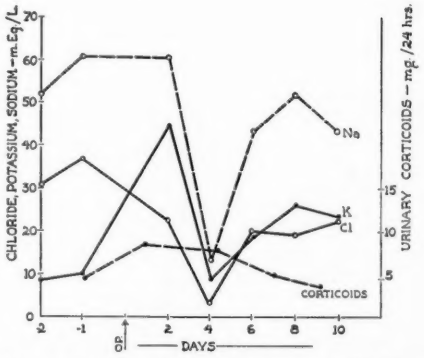

Fig. 3. Correlation of changes in sweat electrolyte concentration with urinary corticoid excretion in patient W. C. Following operative trauma, the sweat potassium level and the urinary excretion of corticoids increased, followed in 2 days by a decrease in the sodium, potassium, and chloride levels.

increase in potassium excretion in the sweat, followed by a decrease in sodium, potassium, and chloride excretion. These findings in a single patient are fairly typical of the average changes found in 6 additional patients studied by us and in patients studied by others (9).

The relationships between adrenocortical activity and the urinary excretion of nitrogen and preformed creatinine may be seen in Figures 5, 6, and 7. In general, the curves for the urinary excretion of steroids, especially of corticoids, were similar to those for nitrogen and creatinine excretion. Major operations were followed by an increase in the urinary excretion of preformed creatinine, nitrogen, and corticoids.

DISCUSSION

Steroid excretion and total eosinophil counts. The postoperative excretion of corticoids and 17-ketosteroids reported in this study is in essential agreement with the results of others. As already mentioned, we have found the excretion of 17-ketosteroids increased only irregularly following surgical trauma, and we believe that the measurement of this moiety is less apt to reflect accurately alterations in the level of adrenocortical activity than is the measurement of corticoids.

The inverse relationship which exists postoperatively between the urinary excretion of corticoids and the total eosinophil count has been found to be a common one. Yet, the total eosinophil count can identify only directional alterations in adrenocortical activity; after the count has fallen to zero, further increments in the level of cortical activity are not manifest and, furthermore, the total eosinophil count gives almost no qualitative information regarding which of the corticoids are present in the greatest concentration. The total eosinophil count may not fall following the injection of ACTH in a patient who has marginal but functionally adequate cortical activity; perhaps this is due to the fact that the adrenal remnant is already maximally stimulated by the endogenous ACTH from the patient's own pituitary. However, in spite of these and other considerations previously noted, the total eosinophil count is a practical and useful index of alterations in the level of adrenocortical activity.

Adrenocortical activity and body fluid metabolism. The results presented graphically in Figure 3 are more or less typical of those changes which occur in sweat electrolyte concentrations following trauma, namely, an increase in the level of potassium, with a decrease in that of sodium and chloride. This pattern of electrolyte excretion following injury is found also in the urine; again this is probably, but not necessarily, the result of an increased adrenocortical activity. It is per-

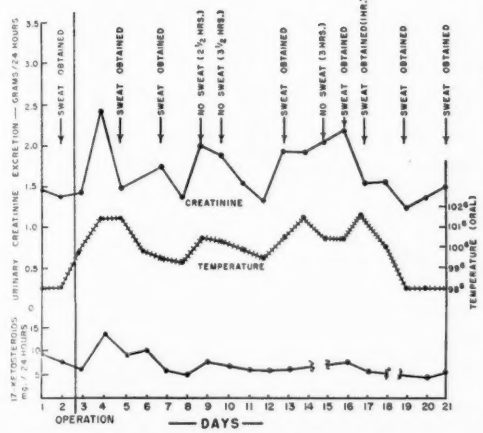

Fig. 4. This graph presents data (patient W. S.) showing relation of sweating to body temperatures and to urinary excretion of creatinine and 17-ketosteroids. There is a fair correlation between the oral temperature and the creatinine excretion. There appears to be no definite relationship between the ability to sweat and the other physiologic measurements presented.

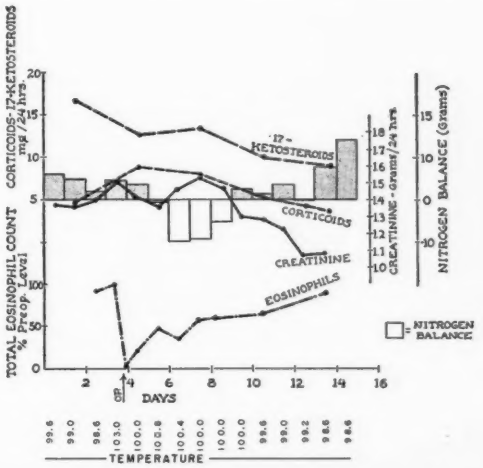

Fig. 5. Chart showing effect of operation on nitrogen balance, total eosinophil counts and urinary excretion of creatinine corticoids and 17-ketosteroids in patient W. C. This patient showed an increase in corticoid excretion following operation. (Each point on the corticoid curve represents the average value for the pooled urines of 3 days.) He presented a markedly negative nitrogen balance on the third, fourth, and fifth postoperative days, and his thyroid activity (not shown) increased to a toxic level postoperatively. Note the initial increase in creatinine excretion the day of operation and the secondary rise several days later associated with the maximal increase in nitrogen excretion. The total eosinophil count returned to the preoperative level at about the same time as did the excretion of corticoids. The maximal daily oral temperatures are given. The brief spike to 103 degrees occurred shortly after the operation had been completed and it was associated with a shaking chill. A minor transfusion reaction was considered to be the most likely cause of this febrile response. Except for this episode, the patient had a reasonably smooth postoperative course. He received 2,100 calories and 150 grams of protein daily except on days 4, 10, 11, and 12, when he received 100, 80, 124, and 70 grams of protein and 800, 1,610, 2,229, and 1,371 calories, respectively.

haps not so generally appreciated that, in addition to alterations in sweat and urine following trauma, there is also a diminished volume of succus entericus, and this too has been correlated with an increase in adrenocortical activity (4).

Steroid excretion, thyroid activity, and nitrogen metabolism. Our patients exhibited an increase in nitrogen excretion following the trauma of operation, a finding demonstrated in experimental animals by Cuthbertson in 1932. The relationships between corticoid excretion and nitrogen excretion, in those patients in whom both were studied, are illustrated in Figures 5, 6, and 7. While the 2 curves for each patient had similar contours, the peak in corticoid excretion usually preceded the peak in nitrogen excretion by a day or so. A direct cause and effect relationship between the increased adrenocortical activity and the increased nitrogen excretion cannot be accepted without reservations. Ingle and Engle have demonstrated similar metabolic changes in adrenalectomized rats subjected to a standard trauma while on constant doses of adrenocortical extract. This suggests that the basic trigger mechanism for the increased nitrogen excretion is not increased adrenocortical activity per se, but is some other factor, though adequate amounts of adrenocortical material are necessary for its manifestation. Further complicating the picture, however, is the fact that cortisone in large doses does produce negative nitrogen balances which can be inhibited by testosterone.

An additional facet of this study was the investigation of the effect of anesthesia and operation on thyroid activity. Measurements were made before and 7 days after operation with both the radioiodine uptake and the con-

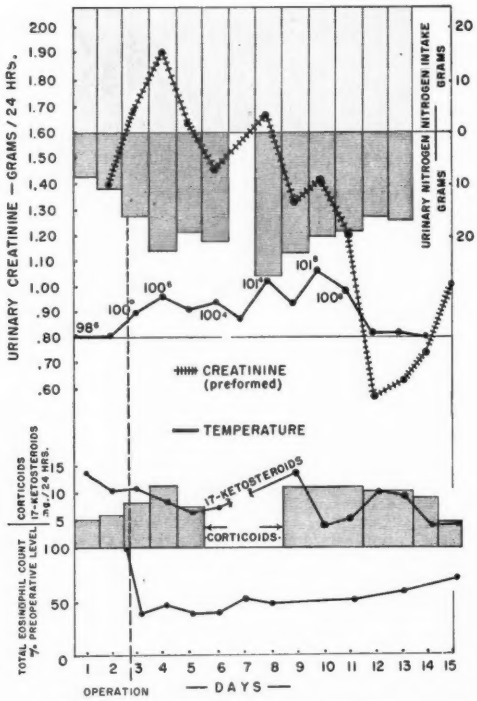

Fig. 6. Chart showing effect of operation (colectomy) on the total eosinophil count, temperature curve, and urinary excretion of nitrogen, creatinine, corticoids and 17-ketosteroids in patient D. C. Measurements are given in apposition so that the several metabolic processes may be readily compared. Following operation there was an increase in the urinary excretion of nitrogen, corticoids, and creatinine, associated with a decrease in the excretion of 17-ketosteroids and in the total eosinophil count. Despite the definite increase in corticoid excretion, the fall in the eosinophil count postoperatively was only moderate considering the magnitude of the trauma. The relationships between the fever, nitrogen, corticoid, and creatinine curves should be noted. So far as the early postoperative period is concerned, all 3 curves are elevated on the day following that in which the operation was performed. Yet, lest it be concluded that the fever was the cause of the increased urinary excretion of these three metabolites, rather than being merely an associated phenomenon, it should be observed that on the tenth day (seventh postoperative day) the maximal oral temperature was associated with a continuing decline in nitrogen and creatinine excretion; corticoid excretion was again elevated. This patient exhibited evidence (radioiodine uptake and radioiodine conversion ratio) on the seventh postoperative day of a pronounced increase in thyroid activity. The reason for the marked decrease in creatinine excretion which occurred on the ninth postoperative day is not clear, though it did herald a return of body temperature, total eosinophil counts, and corticoid excretion to normal levels. A similar type of metabolic response has been observed in other patients. This subject received 150 grams of protein and 2,100 calories daily.

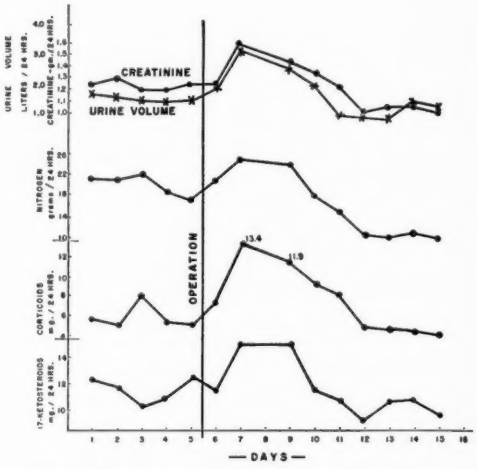

Fig. 7. Chart showing urinary volume and excretion of nitrogen, creatinine, corticoids, and 17-ketosteroids in patient P. D. after gastric resection. The points to be noted are the similarity of the curves representing the urinary excretion of 17-ketosteroids, corticoids, nitrogen, and creatinine. While the excretion of 17-ketosteroids was increased following operation in this patient, an increase was not observed in all patients. The similarity of the curves would, at first glance, appear to indicate that the postoperative increase in the excretion of the four types of metabolites was a function of the increased urinary output. This was not the case. The urinary volume increased a maximum of 110 per cent; the creatinine, nitrogen, corticoid, and 17-ketosteroid excretion increased 34, 20, 51, and 45 per cent, respectively. This patient had a very mild febrile response to operation. At no time did his oral temperature exceed 100 degrees. Certain of the data obtained from the study of this patient have been reported elsewhere (6).

version ratio techniques. These results are reported in some detail elsewhere (1), but it may be noted here that following operation there was evidence of an increase in thyroid activity in patients D. C., W. C., and W. S., but a decrease in patient P. D. The 3 patients whose thyroid activity appeared to have increased exhibited larger negative nitrogen balances than did the patient whose thyroid activity appeared to have decreased. However, the last patient had had an operation approximately 3 weeks earlier and his "deposit" protein may not yet have been replaced. These findings are of particular interest in the light of the report of White and Dougherty, who apparently were able to differentiate between the actions of the thyroid and the adrenals on nitrogen metabolism. Using starvation stress

in mice, these workers found that the adrenal cortex had little effect in mobilizing nitrogen from the muscles.

Adrenocortical activity and creatinine metabolism. There was evidence that the urinary excretion of preformed creatinine is influenced by adrenocortical activity. This was derived from the fact that a patient who required replacement therapy following subtotal adrenalectomy for hypertension excreted very small amounts of creatinine before the therapy was begun; as replacement therapy was administered, these values returned to normal (7). This decreased excretion was considered to reflect a decreased absolute production of creatinine, but a decreased renal clearance of this metabolite was not excluded in this particular patient. In 11 patients who had major operations other than adrenalectomy, the urinary excretion of creatinine was found to be consistently increased following surgery, and there was a direct correlation between creatinine and corticoid excretion in those patients in whom both moieties were measured (6). Evidence against the fact that the increased creatinine excretion in these patients was due solely to an increased renal clearance of this substance was the finding that following operation the serum creatinine levels either remained the same or increased; they rarely decreased. Furthermore, since there was no definite time relationship between the periods of intravenous glucose (and protein hydrolysate) therapy and the postoperative increase in creatinine excretion, it is unlikely that the observed alterations in creatinine metabolism were due to the intravenous administration of these substances. Thus, it would appear that the relationships between adrenocortical activity and creatinine excretion merit further appraisal.

Direction which studies of convalescence may take. There is great need, in studies of convalescence, to identify additional measurable physiologic processes which vary with the patient's symptoms. For instance, we have seen that the urinary corticoid excretion is increased for a time postoperatively, but that the duration of this increase is much less than the duration of weakness and inability to work. Those processes which restore full health and the desire to return to work need to be identified.

SUMMARY AND CONCLUSIONS

1. The effect of major operations on the urinary excretion of corticoids in 4 patients and of 17-ketosteroids in 5 patients has been correlated with certain aspects of nitrogen, creatinine, and electrolyte metabolism. Body temperature changes, total eosinophil counts, certain aspects of nutrition, and thyroid activity have also been examined.

2. The urinary excretion of corticoids increased in all 4 patients so studied. The urinary excretion of 17-ketosteroids increased in 3 of 5 patients so studied.

3. There was a close inverse correlation between the total eosinophil count and the urinary excretion of corticoids following surgery. The eosinophil count decreased as the corticoid excretion increased. This consistent relationship was not observed between the total eosinophil count and the 17-ketosteroid excretion.

4. In most patients, the postoperative increase in corticoid excretion is accompanied by an increase in the sweat potassium concentration and a decrease in the concentration of sodium and chloride.

5. Following operation, the increases in the urinary excretion of corticoids, nitrogen, and creatinine showed similar time relationships. These increases were largely independent of changes in urinary volume.

6. In studies of convalescence there is a need for the identification of additional measurable physiologic processes which can be correlated with the symptoms of the patient.

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GASTROJEJUNOCOLIC FISTULA

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THE definitive therapy of peptic gastrojejunocolic fistula entails two problems: the elimination of the fistula and the correction of the ulcer diathesis. Experience with 8 consecutive unselected cases leads us to believe that both problems can usually be met with the operation performed in one stage.

Much has been written regarding the surgical therapy of this condition. The various procedures may be grouped into two main categories, those designed to eliminate the fistula and restore the continuity of the gastrointestinal tract, and those designed to eliminate the fistula and prevent ulcer recurrence. These have been performed in one or in multiple stages. The restorative operations have consisted in disconnection or excision of the fistula and closure of the component openings in the stomach, jejunum, and colon. The curative type of operation, in addition to excision or dismantling of the fistula, has added to it a procedure designed to correct the patient's basic pathology—the ulcer diathesis. Gastroenterostomy, gastroenterostomy and vagotomy, and subtotal gastrectomy constitute the added procedures that have been recommended. Since many patients with gastrojejunocolic fistula are in poor condition, it is understandable that preliminary operations designed to improve the patient's physical status have been advocated. The two stage procedures have involved jejunostomy, ileostomy, cecostomy, and transverse colostomy. Feeding jejunostomies have lost favor since the advent of the more complete methods of parenteral alimentation. The other preliminary procedures have been devised to prevent reflux of colonic contents into the stomach and jejunum, and thereby control the diarrhea that is a prominent and distressing symptom of most gastrojejunocolic fistulas. Subsequent to publication of Pfeiffer's original paper, colostomy proximal to the fistula became the preferred method. Following cecostomy, a significant portion of the fecal stream continues to gain access to the fistula, and the well known fluid and electrolyte disturbances, secondary to an uncontrolled ileostomy makes this operation a dubious one. In 1943, Lahey and Marshall attempting to prevent contamination of the skin following transverse colostomy, suggested the formation of an ileodescending colostomy as a by-passing procedure. A variation in the usual management of the colonic component of the fistula was also reported by the same authors who for technical ease, included right colectomy along with gastrectomy in the definitive treatment of the fistula.

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CASE REPORTS

CASE 1. A. B., a 37 year old white male, was admitted to the Doctors Hospital complaining of intermittent epigastric pain, weight loss of 20 pounds, and diarrhea for the preceding 4 months. There had been no history of melena, hematemesis, or fecal eructation. Past history revealed that the patient had had plication of a perforated duodenal ulcer 7 years prior to admission, a subtotal gastrectomy 2 years prior to admission, and reresection for a marginal ulcer 11 months prior to the present admission.

Physical and laboratory examinations were negative except for a mild secondary anemia (hemoglobin 12 gm.) and evidence of weight loss. Preoperative preparation consisted of blood transfusion, amigen, and vitamins. Operation consisted of reresection of the stomach, resection of jejunum, and closure of the colonic component of fistula. The postoperative course was uneventful. Follow-up examination 6 years and 4 months postoperatively revealed that the patient was free from symptoms, had regained his weight, and took an unrestricted diet.

CASE 2. J. A., a 53 year old white male, was admitted to the University Hospital with a history of increasing diarrhea, eructation, and gaseous distention for the preceding 5 months. There had been a 25 pound weight loss during this period. Past history revealed that a gastroenterostomy had been performed for peptic ulcer 28 years prior to the present admission. There had been no recurrence of

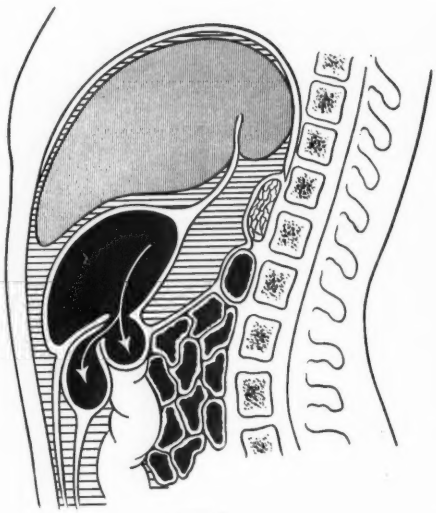


FIG. 1

Fig. 1. Sagittal section of the abdominal cavity illustrating connection of stomach, jejunum, and transverse colon.

ulcer symptoms following operation and the patient had enjoyed good health until the present illness.

Physical examination was essentially negative. Significant laboratory examination revealed a hemoglobin of 13 grams, and a plasma protein level of 5.9 grams. There was no free acid in the stomach and no free acid was obtained after alcohol or histamine stimulation. Roentgenograms of the abdomen following ingestion of barium were reported as showing a marginal ulcer. Preoperative preparation included blood transfusion, parenteral protein hydrolysate and vitamins, and the oral administration of succinylsulfathiazole. On the tenth hospital day, laparotomy was performed and the patient found to have had a previous pyloric exclusion in addition to a retrocolic gastroenterostomy. At the time of operation there was a gastrojejunocolic fistula and following dissociation of the transverse colon, a 1 centimeter opening in the latter structure was seen. The colon and jejunum were resected and a subtotal gastrectomy with removal of the previously excluded pylorus was performed. The patient's postoperative course was uneventful and he was discharged on the ninth postoperative day. When last seen, 4 years after operation, he had no complaints referable to the gastrointestinal tract and had gained 25 pounds.

CASE 3. A. M., a 60 year old white male, was admitted to the University Hospital with a complaint of 5 to 10 bowel movements per day for the preceding 2 months. The movements occurred 1 to 2 hours after eating. There had been a 47 pound weight loss during the present illness. Past history revealed that an operation had been performed for duodenal ulcer 24 years ago and that 4 years ago the patient had been reoperated upon for gastroduodenal obstruction. The patient had also had a coronary occlusion 3 years prior to the present admission.

Physical examination revealed evidence of recent weight loss and a ventral hernia situated between a right paramedian and a right midline scar. Significant laboratory data included a hemoglobin of 10.9 grams, total protein of 6.5 grams, and a serum chloride level of 525 milligrams per cent. A gastric analysis showed 5 units of free hydrochloric acid in the fasting specimen with a maximum response of 42 units after alcohol. X-ray examination of the abdomen following injection of barium showed rapid entry of clysma into the transverse colon.

Following 1 week of preparation which included blood transfusion, protein hydrolysate infusions, vitamins, and the oral administration of succinylsulfathiazole, operation was performed. A gastrojejunocolic fistula and a duodenal ulcer adherent to the pancreas were found. The previous posterior gastroenterostomy was dismantled and the openings in colon and jejunum closed with 2 layers of nonabsorbable suture material. A subtotal gastrectomy with removal of the duodenal ulcer and a short loop antecolic gastrojejunostomy were performed.

The postoperative course was uncomplicated and the patient was discharged on the ninth day following operation. Follow-up interview 3 years and 6 months later revealed that the patient had gained 35 pounds. There had been no recurrence of ulcer symptoms.

CASE 4. D. A., a 51 year old white male, was admitted to the University Hospital with a chief complaint of diarrhea and a 30 pound weight loss occurring during the 8 months preceding admission. Six years prior to the present admission the patient had undergone subtotal gastrectomy for duodenal ulcer and had been well until the onset of the present illness. During the preceding 8 months there had been an average of 8 to 10 semiliquid stools per day. There had been frequent eructations but no fecal odor had been noted. The patient also complained of intermittent pain in the lower left side of the abdomen.

Physical examination revealed slight abdominal distention and a liver margin palpable 1 fingerbreadth below the costal margin. Abnormal findings included a hemoglobin of 12.2 grams and serum chlorides 445 milligrams per cent. Barium studies of the gastrointestinal tract prior to admission were reported as showing a gastrojejunocolic fistula.

The patient was prepared for surgery with daily protein hydrolysate infusions, vitamins, and oral succinylsulfathiazole. Laparotomy was performed on the fourth hospital day. A huge inflammatory mass involved the region of the fistula. It was necessary to resect approximately 4 inches of transverse colon and approximately 8 inches of jejunum. The ends of the colon and jejunum were anastomosed. A cuff of stomach at the site of the previous gastro-

jejunostomy was also resected and an antecolic gastrojejunostomy performed.

The patient's postoperative course was complicated by an unexplained temperature elevation to 102 to 103 degrees F. for the first 4 days. This fell to a normal level on the fifth day and the patient was discharged on the eighth postoperative day. Interview 3 years and 2 months after discharge revealed that the patient had occasional gnawing sensations, relieved by food, during the night. The patient also stated that he could not consume too much food at one time. He felt that his operation had been successful and he had gained 25 pounds.

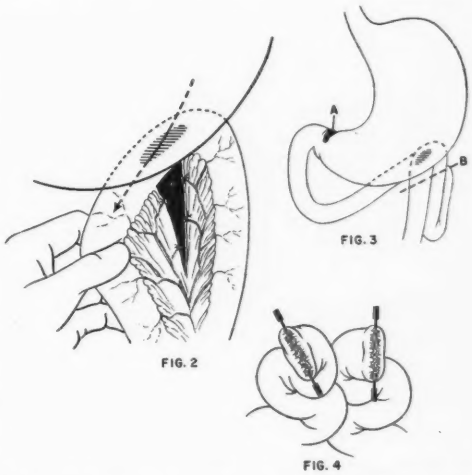
CASE 5. S. P., a 44 year old white male, was admitted to the University Hospital with a 4 months' history of increasing diarrhea, belching of foul material, and weight loss of 15 pounds.

Past history revealed that a gastroenterostomy had been performed for duodenal ulcer 11 years prior to the present illness. The patient was well for 6 months following this procedure and then noted pain in the epigastrium and left upper quadrant. A gastrojejunal ulcer was diagnosed roentgenologically and surgery suggested, but the patient refused. For the next 10 years he was treated by means of diet and antacids and was moderately comfortable until the onset of the present symptoms.

Physical examination revealed a chronically ill patient, with evidence of vitamin B complex deficiency. Laboratory studies revealed a hemoglobin of 14.1 grams and a red blood count of 4.5 million. Total plasma proteins were 6.5 grams per cent, and the serum chlorides were 525 milligrams per cent. Preoperative treatment consisted of a high protein diet, blood transfusion, protein hydrolysate infusion and the administration of vitamins. Aureomycin was given for intestinal antibiosis. Eight days after admission the patient was operated upon. The scar of the old ulcer was present in the duodenum. There was a gastrojejunocolic fistula present that admitted the index finger, and continuous with the fistula, on the jejunum there was an ulcer approximately 1 centimeter in diameter. The stomach, gastroenterostomy, and transverse colon were fused into a large inflammatory mass of the consistency of cartilage. A block resection of the transverse colon, jejunum, and distal two thirds of the stomach including the old duodenal ulcer was performed. The colon and jejunum were anastomosed, and an antecolic gastrojejunostomy was then performed.

The patient made an uneventful recovery and was discharged from the hospital on the ninth postoperative day. By the third postoperative week the patient had gained 14 pounds. During the ninth postoperative week he was readmitted to the hospital for therapy of a posttransfusion homologous serum jaundice. Recovery was uneventful from this disease, and 26 months postoperatively he had gained 35 pounds. He is free from symptoms and eats an unrestricted diet.

CASE 6. S. P., a 52 year old white male, was admitted to Bellevue Hospital complaining of weight



Figs. 2, 3, and 4. Division of the jejunal mesentery and the points of division of the jejunum proximal and distal to the gastrojejunostomy site (line *B*). The cut ends of jejunum held by Furniss pins are shown in Figure 4.

loss of 46 pounds, intermittent epigastric pain, and vomiting for the preceding 6 months. The vomitus had been brownish and fecal in odor. He had also noted fecal eructation. Past history revealed that the patient had had a gastroenterostomy 15 years ago for duodenal ulcer. Ten years ago he had been hospitalized for 6 weeks because of melena and hematemesis. Following this episode he had been well until the onset of his present illness.

Physical examination revealed a malnourished middle aged white male with essentially negative physical findings. Significant laboratory studies revealed a hemoglobin of 13 grams, plasma protein level of 5.7 grams, and serum chloride level of 492 milligrams per cent. Barium enema outlined both the colon and stomach. The administration of barium by mouth revealed free passage of barium between stomach and colon. Gastric analysis revealed 40 units of free acid rising to 65 units ½ hour after histamine stimulation.

Following intensive preoperative dietary therapy, blood transfusions, correction of hypochloremia, and preparation of the large bowel with succinylsulfathiazole, the patient was explored. A previous retrocolic gastrojejunostomy was found. The midportion of the transverse colon was adherent to the anastomotic site. The patient also had a duodenal ulcer. The fistula and adjacent jejunum and transverse colon were excised en bloc and a subtotal gastrectomy, including the old duodenal ulcer, was performed. The ends of the jejunum and transverse colon were anastomosed and an antecolic gastrojejunostomy was performed. The specimen showed a fistula between stomach, jejunum, and transverse colon. The

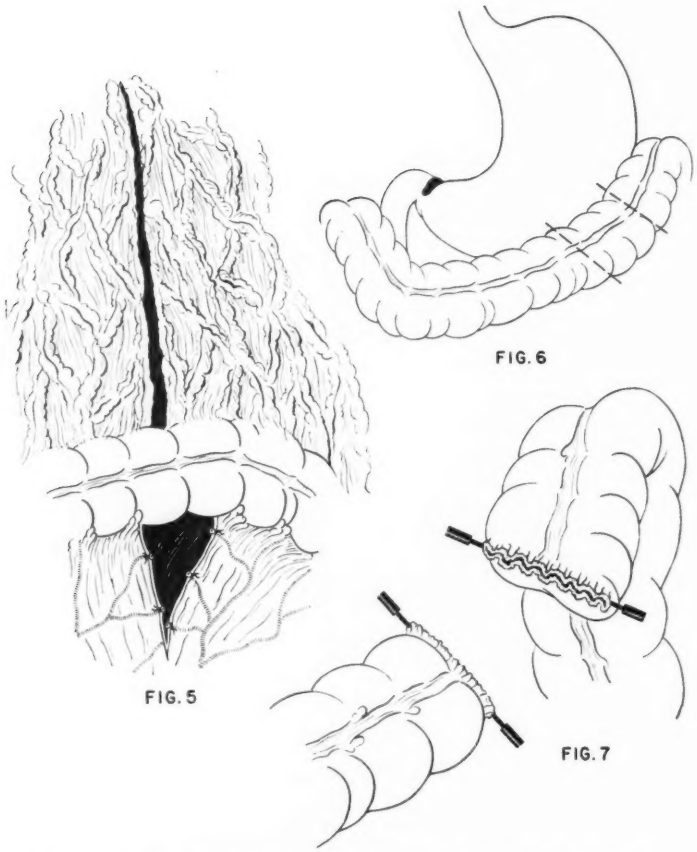


FIG. 5

FIG. 6

FIG. 7

Figs. 5, 6, and 7. Method of handling the colonic component of the fistula.

duodenal ulcer had completely obstructed the first portion of the duodenum. The patient's postoperative course was uncomplicated and he had gained 46 pounds during the first 8 months after discharge.

CASE 7. W. B., a 53 year old white male, was admitted to the University Hospital complaining of diarrhea for the preceding month. The patient also complained of postprandial epigastric distress, eructation, and anorexia. He had occasional vomiting after meals for 1 week prior to admission, but there had been no blood in, or fecal odor to, the vomitus. There had been a weight loss of 27 pounds in the preceding year. Past history revealed that an operation had been performed for bleeding ulcer at another hospital 7 years previously. Since that time he had followed a medical ulcer regimen and had been relatively asymptomatic.

Physical examination was essentially negative. Laboratory data included a hemoglobin of 14 grams, red blood count of 4.5 million, hematocrit of 46 per cent, and a total protein level of 6.0 grams. X-ray studies following showed a gastrojejunostomy and entry of the barium from the transverse colon to the stomach.

Laparotomy was performed on the fifth hospital day following preparation with blood, daily protein hydrolysate infusions, vitamins, and succinylsulfathiazole. At operation a gastrojejunocolic fistula was found. The transverse colon was dissociated and the opening in the colon closed. The jejunum was disconnected from the stomach and similarly closed. A subtotal gastrectomy removing approximately 70 per cent of the stomach and an antecolic gastrojejunostomy were performed. The patient's postoperative course was uneventful and he was discharged on the tenth day after operation. Follow-up interview 8 months later disclosed that the patient had had an occasional episode of diarrhea. He had noted

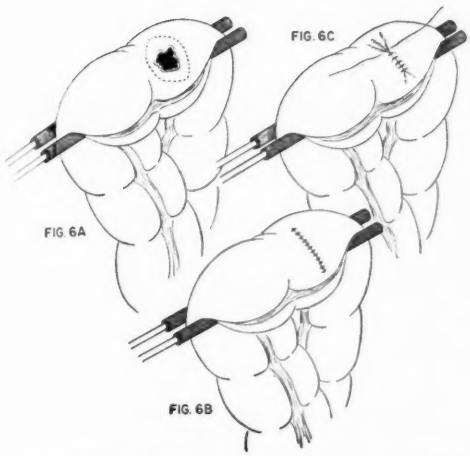


Fig. 6. A, B, and C. Closure of the opening in the transverse colon if this alternative method to block resection is preferred. In certain cases a similar technique may be applied to the jejunum.

no pain, was taking an unrestricted diet, and had gained 10 pounds in weight.

CASE 8. T. K., a 54 year old white male, was admitted to the University Hospital with a history of intermittent epigastric pain for 1 year, constant pain in the lower abdomen for 3 weeks, and hematemesis and melena for 1 day.

Past history revealed that the patient had had a subtotal gastrectomy for duodenal ulcer at another hospital 3 years prior to the present admission. He had been well following this operation until the onset of his present symptoms. There had been no weight loss.

Physical examination was essentially negative. Significant laboratory studies revealed a hemoglobin of 11.5 grams and a red blood count of 4.2 million. Roentgenograms following the ingestion of barium revealed a stomal ulcer. No clysma was seen in the colon, however. The patient continued to pass old and fresh blood per rectum for the first 24 hours in the hospital. On the third hospital day the hemoglobin had fallen to 10.2 grams, and the red blood count to 3.7 million. The patient was prepared for operation with daily protein hydrolysate infusions, parenteral vitamins, and blood transfusion. Laparotomy was performed on the sixth hospital day and the patient was found to have a marginal ulcer which had perforated into the transverse colon. The previously constructed gastrojejunostomy was retrocolic. The perforation was approximately 1 centimeter in diameter. The stomach was disconnected from the jejunum, and about 3 inches of stomach reresected. The jejunum was disconnected from the transverse colon and that portion of jejunum involved in the fistula was resected. The ends of the

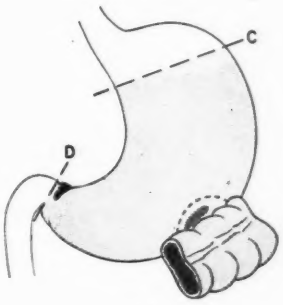


FIG. 8

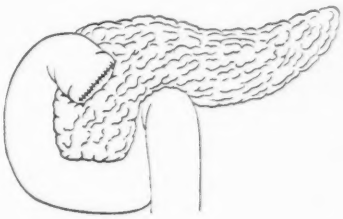


FIG. 9

Fig. 8. Portion of the stomach, with attached segments of jejunum and transverse colon to be resected.
Fig. 9. The closed duodenal stump following removal of the specimen.

jejunum were anastomosed. The opening in the transverse colon was closed. An antecolic gastrojejunostomy was then performed. The patient's postoperative course was uneventful and he was discharged on the tenth postoperative day. Interview 6 months later revealed that the patient was eating a normal diet and had no complaints referable to his gastrointestinal tract.

A review of the literature of the past decade reveals that more than 50 per cent of the patients having restorative procedures without inclusion of an operation for the ulcer diathesia, have had recurrence of symptoms of either fistula, marginal ulcer, or the original ulcer. A review of the patients having a definitive operation for ulcer as well as treatment of the fistula reveals a failure in but 4 per cent. The results of restorative and curative operations for gastrojejunocolic fistula in 115 cases compiled from the literature of the past 10 years, including the author's

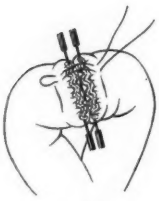


FIG. 10

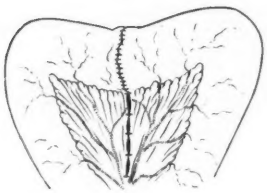


FIG. 11

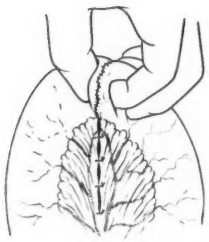


FIG. 12

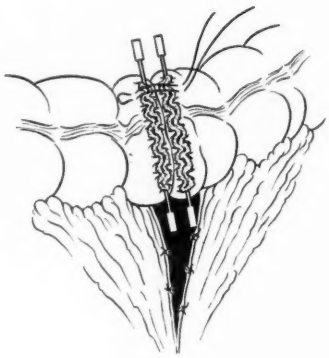


FIG. 13

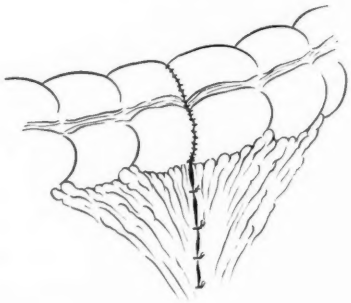


FIG. 14

Figs. 10, 11, and 12. Method of anastomosis of the jejunum and closure of the jejunal mesentery. The anastomosis is performed with one layer of interrupted Halsted mattress sutures of cotton.

Figs. 13 and 14. Reconstruction of the transverse colon by a similar technique.

cases, show that 33 patients had restorative operations (disconnection of fistula with restoration of continuity) with 14 or 42 per cent good results and 19 or 58 per cent poor results. Curative operations in addition to elimination of the fistula consisted of the following: gastrectomy on 75 patients with 72 (96 per cent) good results and 3 (4 per cent) poor results, gastroenterostomy on 6 patients with 4 good results (66 per cent) and 2 poor (33 per cent), and gastroenterostomy plus vagotomy in 1 with a good result. All operative and hospital deaths during the postoperative period were excluded. In the 8 cases reported, all patients having subtotal gastrectomy or reresection of the stomach as well as surgery for the fistula in one stage, the results have all been good over a follow-up period varying from 6 months to 6 years and 4 months, with an average of 2 years and 3 months.

The problem of multiple stage surgery in these patients is principally one of mortality The mortality in the largest series varied from 12 to 43 per cent, with a slightly higher average mortality for definitive operations performed in one stage than those with a preliminary transverse colostomy. Our experience without a mortality in 8 unselected consecutive cases done in one stage suggests a greater degree of safety than that indicated in the literature. We believe that aggressive pre-

operative preparation designed to correct both fluid and electrolyte disturbances, anemia, avitaminosis, mineral deficiency, and protein depletion can convert most of these patients into adequate surgical risks for one stage definitive surgery. The colon is prepared for surgery with a suitable antibiotic. It is obvious that good anesthesia, blood replacement, and experienced surgical hands are essential during the operation.

The technical aspects of the operation are illustrated in Figures 1 to 15. For the large fistula with inflammation and induration of the jejunum and colon, the resection of these structures to the level of normal intestine between Furniss clamps (Figs. 2 to 7) keeps contamination at a minimum and avoids the difficulties inherent in attempting to separate large fixed inflammatory masses. The fistula, the involved colon, and jejunum are left attached to the stomach (Fig. 8). For small fistulas with little induration, the jejunum and colon can be separated and the openings closed (Figs. 6 A, B, C). Most of our surgery on the small and large gut is done with Furniss clamps, and the anastomosis performed over two Furniss pins with one layer of interrupted mattress sutures of cotton (Figs. 10 to 12). The gastrectomy involves two-thirds to three-fourths resection and includes the entire pylorus and the ulcer.

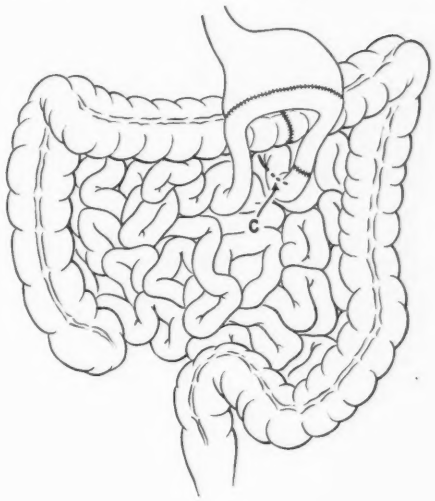


FIG. 15

Fig. 15. The gastrojejunostomy is an antecolic Polya type. This is placed just distal to the jejunal anastomosis. The colonic anastomosis lies behind the jejunal mesentery *C* represents the ligament of Treitz.

DISCUSSION

Our experience, together with that in the literature, would indicate that the simple disconnection of the fistula is poor definitive therapy for gastrojejunocolic fistula. Fifty-eight per cent of recurrence of symptoms as compared to 4 per cent is convincing data. We believe that subtotal gastrectomy or re-resection should be uniformly practiced in the therapy of this condition.

The steps of the pathogenesis of gastrojejunocolic fistula include any type of gastric surgery with a subsequent marginal ulcer and fistula. It would appear that disconnection of the fistula with the formation of a new gastrojejunostomy would invite the same sequence of events responsible for the original lesion. Vagotomy, while recently suggested in conjunction with gastroenterostomy as a definitive procedure after dissociation, may be of questionable value. Byrd has recorded 2 cases of fistula developing after vagotomy for marginal ulcer, and Wilbur and associates have stated that as increasing numbers of marginal ulcers are treated by vagotomy the number of gastrojejunocolic fistulas might increase.

The question of one stage versus two or three stage operations in this condition continues. From the patient's point of view the one stage operation with its shorter period of hospitalization, a single operation, and the elimination of a colostomy is preferable. As a result of the recent refinements in the preoperative preparation of debilitated patients for surgery, and the improvement in anesthetic techniques, we feel that an increasing number of patients may be treated successfully without resort to preliminary colostomy.

SUMMARY

Eight unselected consecutive cases of patients with peptic gastrojejunocolic fistula operated upon in one stage without mortality

are presented. The importance of subtotal gastrectomy in the definitive treatment of the fistula is emphasized. The operative technique is reviewed.

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SUBPHRENIC ABSCESS

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ABSCESS in the subphrenic region is an important and serious surgical infection. Fortunately the condition is relatively uncommon. Although subphrenic infections share many of the properties common to surgical infections in general, they also possess facets of special interest to the surgeon. The unique location of the subphrenic region serves to complicate the surgical approach. The proximity of the abscess to the pleural cavity and the liver makes for additional hazards. The wide variety of primary diseases in various parts of the body which is responsible for the initiation of subphrenic infections accounts for a complex pathogenesis. Problems in diagnosis of subphrenic abscess are sometimes greatly magnified by a paucity of clinical findings which suggest the correct solution to the clinician. The technical problems involved in establishing effective surgical drainage of the abscess add to the trials of the treatment of the condition. The primary disease frequently persists, and complications of the subphrenic abscess often develop to add to the magnitude of the burden already placed upon the patient.

ANATOMY

The subphrenic region is bounded above by the diaphragm and below by the transverse colon and transverse mesocolon. It includes intraperitoneal and extraperitoneal spaces. The intraperitoneal spaces are the right anterior suprahepatic, right posterior suprahepatic, right subhepatic, left suprahepatic, left anterior infrahepatic, and left posterior infrahepatic spaces (Figs. 1 and 2). The extraperitoneal spaces are actually only potential spaces in the bare area of the liver (right extraperitoneal space) and the posterior aspect of the left diaphragm above the left kidney (left extraperitoneal space).

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MATERIAL AND METHOD

The records of cases in which a diagnosis of subphrenic abscess was made at the Mayo Clinic in the years 1930 to 1949, inclusive, were examined. From this group were selected all cases of subphrenic abscess in which surgical drainage was employed. In this manner 154 cases were obtained. The complete clinical record was studied in each case.

Pathologic material removed at the time of surgical drainage of the subphrenic abscesses was available for study in 24 cases. Sections of this material were prepared for microscopic study by either fixed frozen or paraffin techniques. The sections were stained with Barron's or hematoxylin and eosin stain, and some specimens were stained by special techniques. In 24 cases necropsy reports and preserved tissue were studied.

CLINICAL FINDINGS

The 154 patients in this series included 119 males and 35 females, giving a ratio of 3.4 to 1. The ages ranged from 3 to 77 years, and the majority of the patients were in the fifth and sixth decades of life.

The most frequently recorded initial symptoms were pain (50.6 per cent of cases) and fever (32.5 per cent). Fever occurred during the course of subphrenic infection in almost all cases. Other common symptoms were pain (73.4 per cent), pleurisy (14.3 per cent), and cough (14.3 per cent). The signs most frequently noted at physical examination were tenderness (59.1 per cent), dullness and decreased breath sounds (51.9 per cent), draining sinus (35.1 per cent), and palpable mass (19.5 per cent).

A preoperative roentgenologic study was made in all except 14 patients. The common

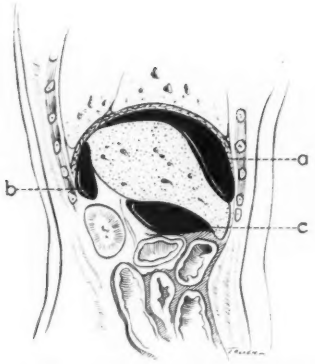

Fig. 1. Sagittal section through the right side of the body illustrating the location of abscesses in the following subphrenic spaces: *a*, right anterior suprahepatic space; *b*, right posterior suprahepatic space; and *c*, right subhepatic space.

findings which aided in the diagnosis of subphrenic abscess included elevation of the diaphragm (60.4 per cent), pleural effusion (44.3 per cent), parenchymal changes in the lungs (30.7 per cent), and gas in the subphrenic region (24.8 per cent). Fluoroscopic examination was helpful in establishing the diagnosis in 17 cases.

The leucocyte count determined prior to operation in 145 cases averaged 14,800 cells per cubic millimeter of blood and ranged from 2,600 to 40,000 cells.

Subphrenic abscess developed as a complication of a surgical procedure in 74 cases; operations on the biliary tract and the stomach accounted for about three fourths of these (Table I). In the other 80 cases the subphrenic abscess was not a complication of a surgical procedure; acute appendicitis and rupture of a duodenal ulcer accounted for the abscesses in 44 cases of this group (Table II).

Bacteriologic studies made in 137 cases indicated that a wide variety of organisms was responsible for the subphrenic infections (Table III). These organisms were isolated mostly from the pus or the tissues removed at the time of drainage of the abscesses, although in a few instances they were cultured from the blood stream or from an empyema complicating a subphrenic infection. Organisms were identified in 131 cases while the

TABLE I.—SURGICAL PROCEDURES WHICH PRECEDED OCCURRENCE OF SUBPHRENIC ABSCESSES

Procedure	No. of cases
Biliary tract	29
Cholecystectomy	19
Operation on common duct	10
Stomach	27
Partial gastrectomy	22
Total gastrectomy	3
Gastroenterostomy	2
Splenectomy	4
Colon	4
Resection, carcinoma	2
Resection, granuloma (foreign body)	1
Colostomy, fecal fistula	1
Pancreas	3
Radical resection, tumor of head	2
Excision, islet cell tumor	1
Diaphragm, repair of hernia; splenectomy	2
Miscellaneous	5
Small Intestine	
Obstruction, release of adhesive bands	1
Volvulus, resection	1
Adrenal cyst, excision	1
Kidney, nephrectomy for chronic pyelonephritis	1
Ovary and fallopian tube, excision for chronic abscess	1
Total	74

results were negative in 6 cases. More than one type of organism was found in 26 cases. The predominant organisms were streptococci (66 cases), Escherichia coli (28 cases), and staphylococci (26 cases).

The subphrenic abscess occurred on the right side in 114 cases, on the left side in 36 cases, and on both sides in 4 cases. Left-sided infections usually followed contamination in the left side of the abdomen but arose from the right side of the abdomen in several instances (perforation of duodenal ulcer in 6 cases and after cholecystectomy in 2). No left subphrenic abscess was attributable to appendicitis. The incidence of involvement of the various anatomic spaces was: on the right side, anterior superior in 73 cases, posterior superior in 49 cases; subhepatic in 25 cases; on the left, superior in 33 cases, anterior in-

TABLE II.—ETIOLOGIC FACTORS, OTHER THAN SURGICAL PROCEDURES THAT PRECEDED THE OCCURRENCE OF SUBPHRENIC ABSCESS

Etiologic factor	No. of cases
...te appendicitis	23
...ture, duodenal ulcer	21
...ease of biliary tract	7
...pture, gallbladder	5
...pture, common duct	2
...ric lesions	4
...pture, malignant ulcer	3
...pture, benign ulcer	1
...ess of liver	5
...damoeba histolytica	3
...ogenic cocci	2
...ma	5
...tured viscus, unknown site	5
...own	4
...llaneous	6
...nal infection	2
...tastasis from femur (osteomyelitis)	1
...teomyelitis, vertebrae L-3, L-4	1
...te gangrenous pancreatitis	1
...ussusception, ileum	1
...	80

...or in 12 cases, posterior inferior in 4 cases, and retroperitoneal in 1 case.

The duration of subphrenic infection was calculated in this study to be the interval in days from the onset of symptoms until surgical drainage was instituted: 1 to 15 days in 25 cases (16.2 per cent); 16 to 30 days in 38 cases (24.7 per cent); 1 to 2 months in 25 cases (16.2 per cent); 2 to 3 months in 10 cases (6.5 per cent); 3 to 6 months in 19 cases (12.4 per cent); 6 to 12 months in 21 cases (13.6 per cent); more than 1 year in 16 cases (10.4 per cent). When the subphrenic abscess followed a surgical procedure the duration of infection was calculated from the date of the surgical procedure regardless of whether the symptoms of a subphrenic lesion developed promptly or not.

Surgical drainage was established within 30 days of the onset of the illness in 63 cases. The average duration of infection for the entire series was 151 days. In one tenth of the cases the duration of infection was longer than 1 year. Subphrenic abscess was already present at the time of the patient's admission to the clinic in 90 cases.

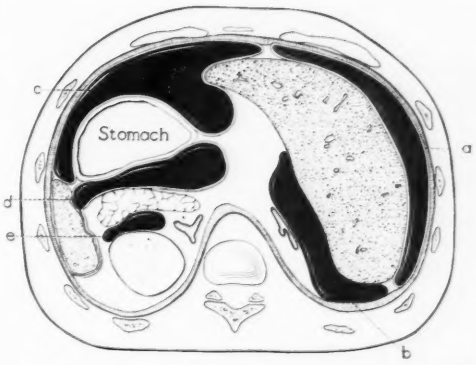

Fig. 2. Diagrammatic cross section of the body through the level of the subphrenic region illustrating the location of abscesses in the following subphrenic spaces: *a*, right anterior suprahepatic space; *b*, right subhepatic space; *c*, left anterior infrahepatic space; *d*, left posterior infrahepatic space; and *e*, left extraperitoneal space.

Eighty-five patients received chemotherapeutic or antibiotic agents as follows: sulfonamide derivatives, 42 patients; penicillin, 51; streptomycin or dihydrostreptomycin, 19; and aureomycin, 2. Some patients received more than one of these agents.

Surgical drainage was established in 160 operations on the 154 patients: extraserous drainage in 72 cases (45 per cent), in 49 (30.6 per cent) of which the surgical approach was anterior, and in 23 (14.4 per cent), posterior; trans-serous drainage in 88 cases (55 per cent) in 57 (35.6 per cent) of which the surgical approach was transperitoneal, and in 31 (19.4 per cent), transpleural. The group of 31 transpleural operations includes 11 operations in which the approach was made through an empyema cavity or the cavity of a pulmonary abscess.

An attempt was made to evaluate the postoperative morbidity by analyzing the duration of postoperative fever and hospitalization. The duration of postoperative fever, calculated from the time of surgical drainage until normal temperatures were maintained regardless of the presence or absence of further complications, averaged 19.3 days for the

TABLE III.—RESULTS OF BACTERIOLOGIC STUDIES IN 137 CASES OF SUBPHRENIC ABSCESS

Organism	No. of cases
Escherichia coli	28
Streptococcus	
Green	18
Hemolytic	14
Faecalis	13
Anaerobic	10
Nonhemolytic	6
Species not identified	5
Staphylococcus	
Aureus	15
Albus	9
Species not identified	2
Gram-negative bacilli	14
Actinomyces bovis	6
Proteus (species not identified)	4
Endamoeba histolytica	3
Mycobacterium tuberculosis	2
Clostridium welchii	3
Aerobacter aerogenes	3
Diplococcus pneumoniae	2
Gram-positive bacillus	1
Bacteroides	1
Negative results	6

entire series. The average duration was 28.2 days for the patients treated in the period 1930 through 1939, 18.1 days for those treated in the period 1940 through 1944, and 12.9 days for those treated in the period 1945 through 1949. Thus the average duration of postoperative fever in the last 5 years of the study was less than half of that in the first 10 years.

The duration of postoperative hospitalization, considered as the interval from the time of surgical drainage of the subphrenic abscess until dismissal from hospital regardless of the presence of other complications which may have prolonged hospitalization, averaged 37.7 days for the entire series. The average duration was 59.6 days for the patients treated in the years 1930 through 1939, 30.8 days for those treated in the years 1940 through 1944, and 25.9 days for those treated in the years 1945 through 1949. Thus the average duration of hospitalization after surgical drainage in the last 5 year period was less than half of that in the first period consisting of 10 years.

COMPLICATIONS

Complications occurred in 106 patients. All complications including relatively small amounts of pleural effusion or slight pneumonitis were tabulated in this study. The incidence of complications by periods was as follows: 1930 through 1939, 74.5 per cent of 47 patients; 1940 through 1944, 73.3 per cent of 47 patients; and 1945 through 1949, 61.7 per cent of 60 patients.

An analysis of the various types of complications according to frequency of occurrence is given in Table IV.

PROGNOSIS

An accurate determination of the number of deaths directly caused by subphrenic infection is quite difficult and for practical purposes impossible. Any attempt at such a determination is fraught with uncertainty because of the fact that the exact role of the subphrenic infection as a cause of death is sometimes difficult to evaluate. In order to avoid the difficulties of a personal evaluation of the many variable factors it seems most advantageous to include all deaths occurring in patients having a subphrenic abscess. Examples of such deaths included in our mortality studies are massive pulmonary embolus (3 cases), rupture of brain abscess to produce meningitis (2 cases), intestinal obstruction, and infarction of the jejunum.

In the entire series of 154 cases there were 35 deaths, giving a mortality rate of 22.7 per cent. The mortality rate for the group treated in the first 10 years covered by the study was almost two and a half times as high as the rate for the group treated in the last 5 years: among the 47 patients treated during the period from 1930 to 1939 there were 15 deaths (31.9 per cent); among the 47 treated during the period from 1940 to 1944 there were 12 deaths (25.5 per cent); among the 60 treated during the period 1945 to 1949 there were 8 deaths (13.3 per cent).

Whether the subphrenic abscess was situated on the right or left side seemed to have

little bearing on the prognosis. Among the 114 patients with abscess on the right side there were 26 deaths (22.8 per cent), among 36 patients with abscesses on the left side there were 7 deaths (19.4 per cent); and among the 4 patients with bilateral infection there were 2 deaths.

Chemotherapeutic and antibiotic agents were utilized in 83 patients of whom 20 died (24.1 per cent). No such agents were employed in 71 patients of whom 15 died (21.1 per cent).

The type of surgical approach for drainage of a subphrenic abscess has an important bearing on the mortality rate. The most important point in this regard is whether or not a serous cavity is opened in the surgical dissection. Trans-serous drainage was established in 85 patients with 26 deaths (30.6 per cent). Extraserous drainage was performed in 69 patients with 9 deaths (13 per cent). Hence, the mortality rate was nearly two and a half times as high for patients having trans-serous drainage as for those having extraserous drainage.

The presence of complications attributable to subphrenic infection has a profound bearing on prognosis. The death rate for patients with complications was about five times that for patients without complications. During the period 1930 to 1939, among 12 patients without complications who were treated there was 1 death (8.3 per cent); among 35 treated with complications there were 14 deaths (40 per cent). During the period from 1940 to 1944, no deaths occurred in the 13 patients without complications; there were 12 deaths (35.3 per cent) in the 34 with complications. During the period from 1945 to 1949, among 23 patients without complications there were 2 deaths (8.7 per cent); and among the 37 patients with complications there were 6 deaths (16.2 per cent). The mortality rate for the total group of 48 patients without complications was 6.3 per cent, and for the 106 with complications it was 30.2 per cent.

TABLE IV.—COMPLICATIONS OCCURRING IN 154 CASES OF SUBPHRENIC ABSCESS

Complication	Cases	
	Number	Per cent
Pleural effusion	83	54.5
Pneumonitis	60	38.9
Empyema	35	22.7
Bronchopleural fistula	17	11.0
Perforation of diaphragm	10	6.5
Abscess of lung	9	5.8
Atelectasis	9	5.8
Pneumothorax	4	2.6
Pulmonary embolism	3	1.9
Abscess of brain	3	1.9
Perforation into peritoneum	2	1.3
Parotitis	2	1.3
Cerebrospinal meningitis	2	1.3
Pylephlebitis	1	0.6
Septic arthritis	1	0.6
Toxic arthritis	1	0.6
Acute synovitis	1	0.6

PATHOLOGIC FINDINGS

Sinus tracts excised at the time of surgical drainage of subphrenic abscess in 5 patients presented a histologic pattern of chronic inflammatory reaction in 4 instances, the predominant cell type being the histiocyte. The fifth sinus tract showed an acute inflammatory reaction characterized by the presence of richly vascular and edematous granulation tissue and scattered areas of suppurative necrosis.

In 21 necropsy cases the parenchyma of the liver showed all gradations of inflammatory change from mild vascular congestion, edema, and scattered distribution of lymphocytes to severe reactions with areas of hepatic necrosis. The veins in the liver may be involved in the

TABLE V.—PERCENTAGE DISTRIBUTION OF SUBPHRENIC ABSCESSES ACCORDING TO THE MOST COMMON SOURCES OF INFECTION AS REPORTED BY SEVERAL INVESTIGATORS

Source	Lockwood (100 cases)	Whipple (1,000 cases)	Gogol (50 cases)	Faxon (3)(124 cases)	Hochberg (6)(139 cases)	Present series (154 cases)
Appendix	22	21	26	31	21	15
Stomach and duodenum	22	30	36	30	6	34
Liver and bile passages	33	16	20	29	32	27
Other	23	33	18	20	41	25

Fig. 3. Section of liver showing acute suppurative reaction in a vein. Specimen was removed at necropsy in a case in which abscesses of the liver, bilateral subphrenic abscesses, and multiple abscesses of the brain developed after cholecystectomy. ×35.

septic process owing to the presence of septic emboli or to direct invasion of the veins in the liver. An example of septic pylephlebitis in the liver is shown in Figure 3.

Postmortem examinations were performed in 24 cases. In 15 of the 24 cases there was residual abscess formation in the subphrenic region at necropsy. A residual abscess was present in the subphrenic space that was previously drained in 11 of the 24 cases. Other subphrenic abscesses were found in subphrenic spaces which had not been drained surgically in 10 of the cases. Subphrenic abscesses were found on the left side in 3 cases in which abscesses on the right side had been drained surgically. In no instance was a right subphrenic abscess found at necropsy in drainage of left subphrenic abscesses.

In 8 of the 24 necropsy cases there was pleural effusion and in 9 there was pleural empyema. Fatal pulmonary emboli were present in 2 cases and nonfatal pulmonary emboli in 2. Abscesses were found in the lungs in 8 cases, in the liver in 11, and in the brain in 3. Generalized peritonitis was present in 7 cases.

TABLE VI.—PERCENTAGE INCIDENCE OF THORACIC COMPLICATIONS IN REPORTED SERIES OF CASES OF SUBPHRENIC ABSCESS

	Hochberg(5) (111 cases)	Ochsner and DeBakey (1,380 cases)
Pleurisy or pleural effusion	36	28.1
Empyema	19.2	17.8
Bronchopleural fistula	4.7	10.8
Pulmonary abscess	9.6	1.2
Pneumonitis	12.0	1.6
Pneumothorax	9.6	0.21
Pericarditis	2.4	5.1
Mediastinal abscess	—	0.14

TABLE VII.—PERCENTAGE MORTALITY RATES ACCORDING TO SURGICAL APPROACH IN THE TREATMENT OF SUBPHRENIC ABSCESS

Approach	Ochsner and DeBakey, 1938		Hochberg (5) 1938 (90 cases)	Wellman and Maddock, 1939 (39 cases)	Faxon (2), 1940 (111 cases)	Present series (154 cases)
	Collected (932 cases)	Personal (75 cases)				
Extraserous	20.8	10.8	8.5	40	27	13.0
Transperitoneal	35.1	50.0	58.1	59	55	22.2
Transpleural	36.2	42.8	42.6	50	41	43.3

COMMENT

Subphrenic infections arise from sources in many parts of the body but the great majority follow intra-abdominal disease and operations (Table V). The diagnosis of subphrenic infections is sometimes quite difficult. Delay may often result from failure to suspect the possibility of the presence of such an infection. The average duration of infection until treatment in several reported series was: 26 days, 11.6 weeks, 12 weeks, 4 months, and 4.5 months.

Surgical drainage is indicated when suppuration occurs in the subphrenic region. The operation of choice for abscesses which can be

reached by the posterior route is the retroperitoneal approach described by Nather in 1922 (8), and by Nather and Ochsner (9) in the following year. The extraserous abdominal route of Clairmont and Meyer is the procedure of choice for draining abscesses which may be reached via the anterior route.

Complications of subphrenic abscesses play a prominent role in the morbidity and mortality of this disease. The great majority of complications are intrathoracic (Table VI). Thoracic complications have been reported in per cent of 59 cases, 74 per cent of 31 cases, and 61 per cent of 111 cases.

The prognosis, apart from factors such as the inevitably fatal primary pathologic process, the general resistance of the patient, and the virulence of the infecting organism, is influenced by several other factors. Delay in treatment and the presence of complications have a profound bearing. The type of surgical treatment employed also has an important bearing, as evidenced by the fact that in all reported series the mortality rate is significantly higher with a trans-serous than with an extraserous approach (Table VII).

SUMMARY AND CONCLUSIONS

This paper is a report on the study of 154 consecutive cases of subphrenic abscess receiving surgical treatment at the Mayo Clinic over a recent 20 year period.

In this series the ratio of males to females was 3.4 to 1. The most common symptoms of subphrenic abscess were pain and fever. Physical signs of frequent occurrence included tenderness, percussion dullness, and decreased breath sounds over the lower adjacent part of the thorax, and the presence of a postoperative or spontaneously occurring sinus tract. Common roentgenologic findings were elevation of the diaphragm, pleural effusion, parenchymal changes in the lungs, and the presence of subphrenic gas.

The subphrenic abscess developed as a complication of a surgical procedure in nearly half the cases, operations on the biliary tract and stomach accounting for most of these. In a little more than half the cases the subphrenic abscess was not a complication of a surgical procedure, appendicitis and rupture of a duodenal ulcer being the more common causes of the abscess in this group.

It was observed that the average duration of postoperative fever and postoperative hospitalization during a recent 5 year interval was less than half that of an earlier interval covered by the study, before chemotherapeutic and antibiotic agents were freely available.

Complications attributable to subphrenic infection occurred in about two thirds of the cases. The most common complications were pleural effusion, pneumonitis, empyema, and bronchopleural fistula.

Death occurred in a little more than a fifth of the cases. There was, however, reduction in death rate over the 20 year period as evidenced by the fact that the rate for the early years covered by the study was almost two and a half times as great as the rate for the more recent years. The mortality rates were similar for abscesses on the right and left sides.

When a trans-serous approach was used the death rate was approximately twice as high as when an extraserous approach was used. Also, when complications were present the death rate was about five times as high as it was when they were absent.

On the basis of observations made in 24 cases in which necropsy was performed, it would appear that failure of a patient to achieve expected improvement after surgical drainage of a subphrenic abscess may be due to the presence of abscesses in other subphrenic spaces.

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A NEW TECHNIQUE OF VENOGRAPHY OF THE LOWER EXTREMITIES WITH UROKON

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DURING the past 28 years numerous techniques have been described for roentgenography of the veins in the lower extremities. These methods have varied from fluoroscopic visualization to complex surgical procedures, but all have been based on the principle of distal injection; that is, the contrast medium has been injected into the peripheral vascular system at a point distal to the area of suspected pathologic change. To visualization of the vessels in the leg the injections of media have been in the ankle.

Venography of the lower extremities was first performed by Berberich and Hirsch and was later accorded a brief popularity following the publications of Dos Santos and Bauer (1, 2). Their technique of canalization of the small saphenous vein posterior to the lateral malleolus required a minor surgical procedure and resulted in failure to produce uniformly reliable venograms, particularly in the femoroiliac region. More recently Ferreira and associates have described a method of "dynamic phlebography" which involved passing a catheter up the exposed lesser saphenous vein to the popliteal space where it entered the deep venous system. Following injection of the contrast medium, an x-ray exposure was made. The patient was then instructed to flex the knee and extend the foot, and a second x-ray exposure was made in an effort to determine possible incompetence of the deep venous systems as evidenced by failure to empty after contraction of the patient's gastrocnemius muscles. Mahorner and Scott have independently described methods of utilizing a tourniquet to constrict the superficial veins of the lower leg and thus force the contrast medium into the deep veins of the leg following injection of the dorsal vein of the foot. None of these methods has been accorded widespread clinical application because a satisfactory radiopaque medium was not available and they too often required cumbersome surgical exposure and local anesthesia with attendant risk to the seriously ill patient.

It is the purpose of this report to call attention to the superior qualities of buffered 70 per cent urokon as a contrast medium for venography and to describe a simple technique for proximal injection of the contrast medium which has resulted in roentgenologic visualization of the veins of the pelvis and lower extremities.

DETAILS OF INJECTION TECHNIQUE FOR VENOGRAPHY

The opaque medium used in the present group of 87 patients was buffered 70 per cent urokon sodium[1] which is far superior in contrast properties and in low tissue toxicity to any other medium previously available. The 30 per cent solution has been widely used in excretory urography with an exceedingly low incidence of toxic reactions. This material has been used at the University of Virginia in 1,340 consecutive patients for excretory urography with no reaction more serious than mild nausea and occasional vomiting. The 70 per cent solution was developed primarily for use in angiocardiography and translumbar arteriography, but it has also been used for intravenous urography and in children by subcutaneous injection. The toxicity of the buffered 70 per cent solution is exceedingly low, and it has been demonstrated to produce either an almost imperceptible or no inflammatory reaction following intramuscular injection as judged by histologic examination of the tissues. Dotter

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[1]A sodium salt composed of 3 acetylamino 2, 4, 6,-tri-iodobenzoic acid which contains 65.8 per cent iodine.

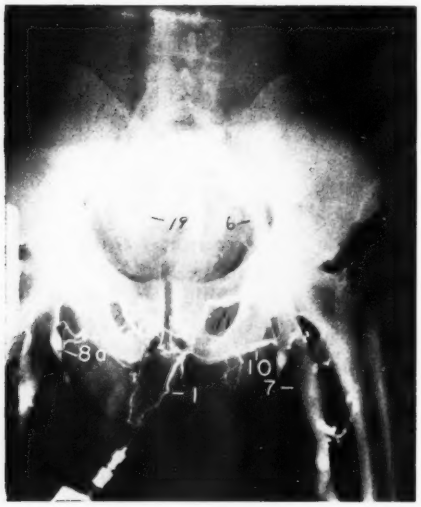

Fig. 1. Normal venogram of femoroiliac veins. Bilateral filling occurs in 54 per cent of normal cases with single injections of superficial median dorsal vein of penis.

TABLE 1.—KEY TO VARIOUS VEINS INDICATED IN ILLUSTRATIONS

1, Median dorsal superficial vein of penis
2, Lateral dorsal superficial vein of penis
3, Normal valve
4, Incompetent valve
5, Extravascular extravasation
6, External iliac vein
7, Femoral vein
8, Great saphenous vein
  a, Saphenous bulb
9, Profunda vein
  a, 1st perforating branch
  b, 2nd perforating branch
  c, 3rd perforating branch
  d, Lateral circumflex branch
10, Superficial external pudendal
11, Deep external pudendal
12, Superior gluteal
13, Superficial circumflex iliac
14, Anastomotica magna
15, Ascending lumbar vein
16, Small saphenous
17, Recanalized thrombus
18, Paravertebral (Batson's) plexus
19, Sacral plexus
20, Inferior gluteal vein

has employed 70 per cent urokon in 50 cubic centimeter doses administered in less than 2 seconds for angiocardiography in 260 patients (474 injections) without a fatality or serious reaction. The maximum quantity administered to any one patient in this series was 150 cubic centimeters within a period of 1 hour. Urokon sodium is the sodium salt of 3 acetylamino 2, 4, 6,-tri-iodobenzoic acid which contains 65.8 per cent iodine (a concentration 10 to 15 per cent higher than any other iodine compound available for venography). The solution is stable over a wide range of temperature and is buffered to a *p*H of 7.2.

The technique of proximal injection of this contrast medium is based upon the physical properties of this medium. The buffered 70 per cent urokon is readily miscible with the blood plasma, and its high specific gravity of 1.468 as compared to 1.050 for whole blood and 1.020 for blood plasma will result in the gravitation of the contrast medium down a dependent vein and opposite to blood flow to the first competent valve. Thus, the proximal injection technique has physiologic implications which cannot be ascertained by the distal injection methods. Excellent nephrograms and excretory urograms are also obtained by roentgen exposures of the renal areas made at proper time intervals following venography with 70 per cent urokon.

Sensitivity to the contrast medium is tested by 1 drop of the undiluted material held beneath the tongue for 5 minutes followed by the intravenous administration of 1 cubic centimeter of 70 per cent urokon and 10 cubic centimeters of saline administered slowly over a period of 1 minute prior to injection. Although no untoward reactions were observed in this series, the conjunctival and intradermal tests of sensitivity are considered less reliable than intravenous tests and are not recommended for 70 per cent urokon.

The patient is placed in the supine position with the head of the table elevated 15 degrees from horizontal and the bony pelvis centered over a 14 by 17 inch x-ray film. Fifty cubic centimeters of 70 per cent urokon is then injected into the superficial dorsal median vein of the penis, a size 21 or 23 gauge needle being used. The total time for the injection requires 1½ to 3 minutes. The x-ray exposure is made as the injection is completed and this film is developed immediately. If there is a failure to fill femoroiliac systems on both

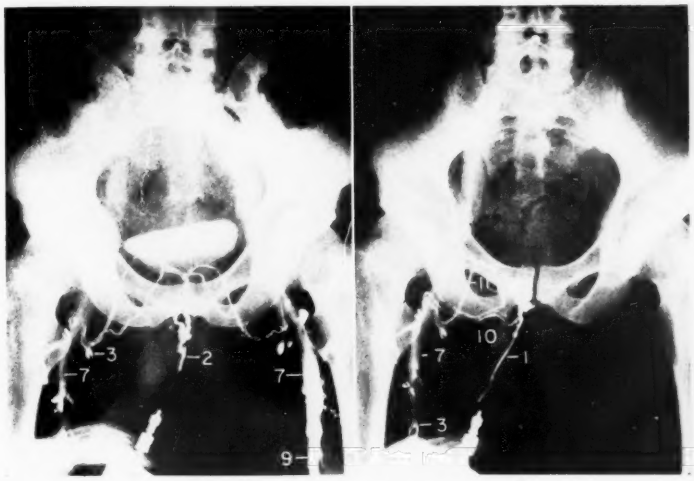

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Fig. 2. a, Unilateral filling following injection of the median dorsal superficial vein of the penis. This occurs in 46 per cent of normals. b, Same patient following injection of the left lateral superficial vein of the penis.

...es, a second exposure is made following ...ection of 25 cubic centimeters of contrast ...dium into the superficial lateral vein of ... penis on the side which failed to be visual... d. The superficial dorsal vein of the penis ...ually drains into the saphenous veins of ...th sides, whereas each lateral vein of the ...nis empties into the ipsilateral side. In the ...rmal supine individual the dye is so rapidly ...moved that the x-ray exposure must be ...ade the moment the injection is completed.

Immediate digital pressure must be applied over the site of the venous puncture to prevent hematoma formation and the possibility of an inflammatory response in the loose areolar tissue of the penis. At the first sign of any accidental local extravasation of the medium, injection should be immediately stopped and the area infiltrated with hyaluronidase.

Bilateral filling, of course, cannot be obtained in the female patient, but unilateral filling may be obtained by the injection of 25 cubic centimeters of the contrast medium into the superficial circumflex iliac or any other superficial vein which empties into the saphenous or deep femoral vein in the thigh.

Venograms of the complete thigh and lower leg may be obtained by the proximal injection technique only when superficial or deep venous incompetence is present. The patient is placed in a semierect position (20 to 45 degrees from vertical) and the contrast material injected into either the median superficial or the lateral superficial vein of the penis as already described. Roentgenograms are made over the thigh and lower leg immediately following the injection. The exposure of the thigh should be made immediately after the injection and exposure of the lower leg made as quickly as the casette and x-ray tube can be changed. Under these conditions the urokon, being heavier than blood, will graviate to the level of the first competent valve of the femoral vein. The large profunda femoris vein is without valves at the point of juncture with the femoral vein and is visualized in 97 per cent of normal individuals. The patient must be cautioned not to move the leg during this procedure as this may empty a competent venous system of contrast material before the roentgenogram can be made. In the normal individual the urokon does not migrate beyond the superior or first competent valve which is usually present in the upper ⅓ of the femoral vein (Fig. 2). The presence of the dye below this

Fig. 3. Venogram obtained after injection of the deep dorsal vein of the penis. Note filling of prostatic plexus and internal hypogastrics.

valve is evidence of incompetence in the deep systems (Figs. 8, 9, and 10). Incompetence of the great saphenous vein with a reversal of blood flow usually results in a majority of the dye passing down the leg by this more superficial route (Fig. 10a). Digital compression or tourniquet lightly applied to the saphenous below the fossa ovalis will direct the flow of contrast medium into the deep venous system under these circumstances (Fig. 10b). If the urokon is permitted to migrate into the lower leg through incompetent superficial veins, an indication of the competence of the deep system can be obtained by having the patient flex the knee and then repeating the roentogenograms of the lower leg as suggested by Ferreira and associates. Complete emptying of the deep venous system will occur in a normal individual.

VARIATIONS IN TECHNIQUE FOR SPECIFIC PROBLEMS

Injection of the contrast medium directly into the superficial external pudendal vein, the superficial circumflex iliac, or other superficial thigh veins may be necessary or desirable when the penile vein cannot be used for any reason (Figs. 5b and 7b). The utilization of these superficial veins is facilitated in acute thrombosis by the immediate dilatation of the collateral circulation. Injections of the deep dorsal vein of the penis and of the corpora cavernosa are not only difficult procedures but fail to result in satisfactory venograms of the extremities.

Occasionally it may be desirable to confirm the presence of obstruction in the deep venous system through utilization of the distal injection technique. This is best accomplished by application of a tourniquet below the knee and injection of the superficial vein of the foot or ankle as described by Mahorner and more recently by Scott (Fig. 4). It must be borne in mind that this technique will demonstrate only the patency of the venous system and lacks the physiologic implications of valvular competency obtained from films made by the proximal injection technique.

If it is kept in mind that 70 per cent urokon will gravitate into the most dependent veins of a resting extremity, then various combinations of the techniques described can be relied upon to give accurate venograms and reliable information as to the status of the deep and superficial venous drainage from the extremity and within the pelvis of the vast majority of patients.

The contraindications to venography as described are severe renal failure or sensitivity to urokon sodium or iodine. In this series of 94 patients there has been no untoward reaction following injections of doses as great as 150 cubic centimeters of 70 per cent buffered urokon sodium. None of these patients required administration of adrenalin. Some have noted a transient sensation of nausea but only 2 patients vomited. Twenty-two patients complained of pain at the site of injection, but this seemed to be due to the overdistention of a small vein by the forceful injection since the pain disappeared immediately after the injection was discontinued. In the presence of incompetent superficial venous systems with edema of the lower extremities, slight discomfort frequently occurred in the

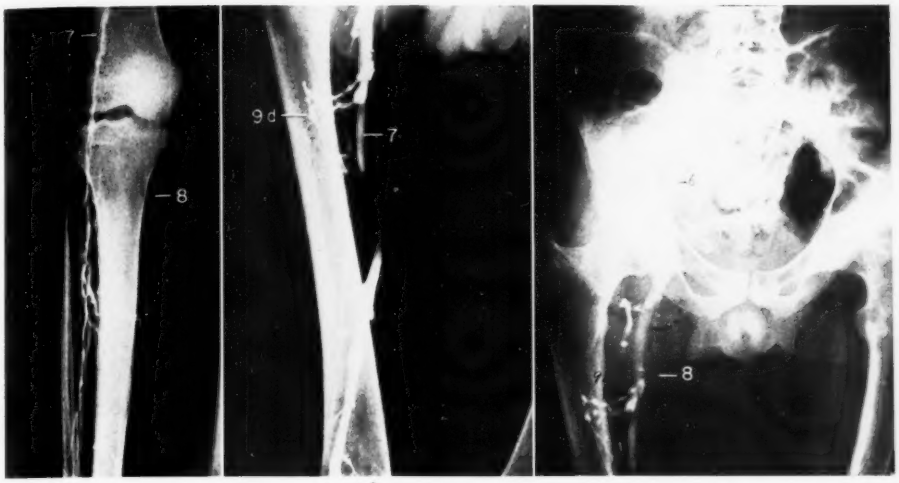

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Fig. 4. Dos Santos technique of distal injection of the lesser saphenous vein with serial films of the leg. a, Urokon is at the level of the knee. b, The femoral vein in the thigh region. Note absence of demonstration of the profunda vein. c, Femoroiliac veins.

lower leg. Movement of the leg immediately relieved this discomfort which seemed to be due to hydrostatic pressure changes within the venous system. There has been no evidence of troublesome thrombosis of normal veins or accelerated propagation of an existing thrombus following the technique as described. Failure to apply pressure to the site of venipuncture has resulted in a large hematoma formation in 2 individuals, and extravasation of the material into the subcutaneous tissues has resulted in a painful inflammatory response in 3 individuals. No permanent scar or disability has been observed to follow any of these complications. Such sequelae are now easily avoided by use of careful technique.

RESULTS IN 94 INDIVIDUALS SUBJECTED TO VENOGRAPHY BY THE PROXIMAL INJECTION TECHNIQUE

Bilateral roentgenographic visualization of the iliac and femoral veins within the pelvic area was obtained in 54 per cent of 78 normal male patients following a single injection of 70 per cent urokon into the superficial median (dorsal) vein of the penis. In the remaining 46 per cent of patients this dorsal vein drained only into either the right or left superficial external pudendal vein so that only unilateral filling occurred. The unfilled side was then visualized in the normal patient by an immediate injection of the superficial lateral penile vein of the unfilled side which invariably drained into the homolateral superficial external pudendal vein. The 70 per cent urokon was found to gravitate into the dependent veins against normal venous flow to the point of competent valves. These competent valves are demonstrated by the clear cut lines of demarcation of the cusps (Fig. 2). On the patient with normal veins and in the semierect position, the urokon will not gravitate beyond the superior valve of the femoral vein. On the other hand, the profunda femoris was observed to fill in 97 per cent of normal individuals. Thus the technique described has proved most successful in demonstrating this latter important vein which is not visualized by any other method of venography (Fig. 4). In every case of so-called normals, a much greater degree of relative incompetency has been noted in the profunda, as contrasted with the femoral vein (compare Figs. 2 and 9). This observation suggests that the valve at the junction of the profunda and femoral veins is usually absent

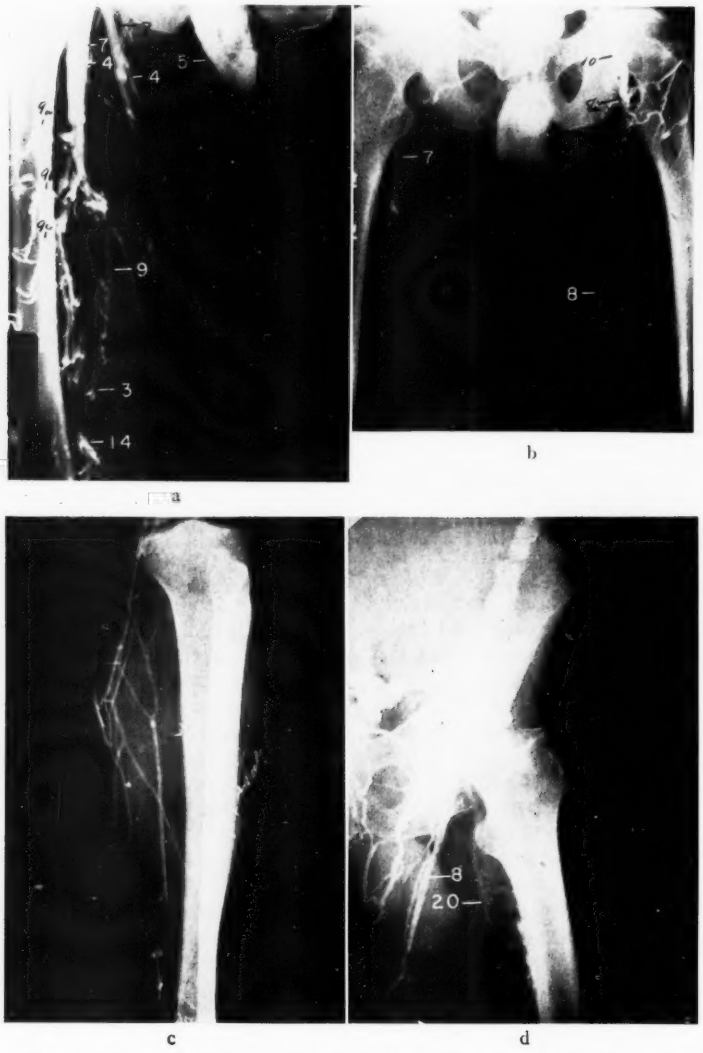
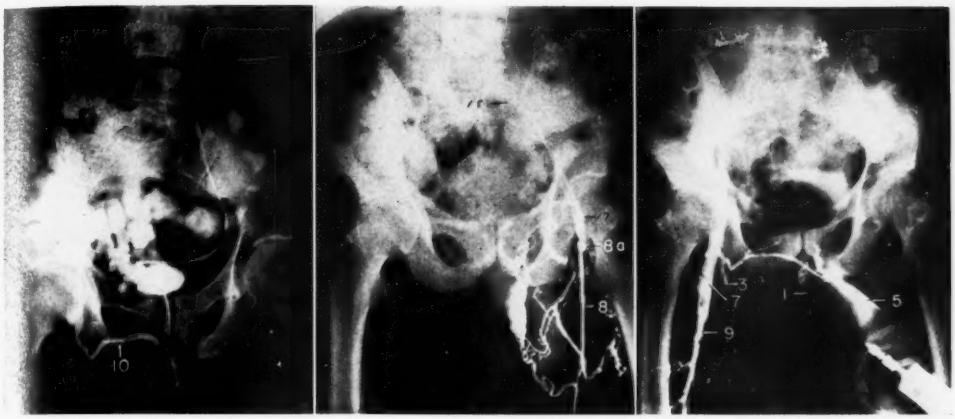


Fig. 5. Patient with left femoroiliac thrombosis and relative incompetence on the right. a, Note absence of filling of veins of left thigh after injection of median dorsal superficial vein of penis. b, Great saphenous vein injected on the left. There is no deep filling and some of the urokon has been directed into the right femoral vein because of reversed blood flow. c, Lesser saphenous vein injected, but deep veins fail to fill. (Compare with Fig. 4.) d, Lesser saphenous vein injected. Only the superficial collateral circulation is filled.

or relatively incompetent. This demonstration naturally raises the question of whether this vein may not be the source of many "silent" pulmonary emboli. The profunda femoris vein does not carry a large current of blood from below the knee which may predispose the blood in this vein to stasis in the bedridden individual. Phlebothrombosis limited



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ig. 6. Patient with left femoroiliac thrombosis. a, e absence of visualization of any veins on left. b, lateral superficial vein of penis injected 6 days after re 6a. Note recanalized thrombus and dilated lumbar paravertebral veins. c, Normal outline of right femoroiliac system after injection of right lateral vein of penis. This vinogram was made at the same time as the one which is illustrated in Figure 6b.

the profunda femoris could not be expected produce the classical Homan's sign, edema, tenderness of the leg. The following illustions are examples of venography by this thod, and Table I is the key to the various ins in all the illustrations.

Figure 1 demonstrates bilateral filling of e femoroiliac veins in a normal young adult ale following injection of 50 cubic centiters of 70 per cent urokon sodium into the perficial median vein of the penis. Figure 2a demonstrates unilateral filling following injection of median dorsal vein of the penis. Figure 2b demonstrates visualization of the femoroiliac systems bilaterally in the same patient following injection of the left lateral vein of the penis with 25 cubic centimeters of 70 per cent urokon sodium. Note the excellent visualization of the large profunda femoris vein on the left.

Figure 3 demonstrates filling of the prostatic, prevesical, internal obturator, and iliac veins following injection of the deep dorsal vein of the penis in a normal young male adult. Injection of the deep dorsal vein of the penis is technically a difficult procedure but usually does not permit visualization of the external iliac or femoral veins.

Figure 4 illustrates the normal venograms of the leg and thigh using 70 per cent urokon and the Dos Santos technique (injection of the lesser saphenous vein). Figure 4a illustrates filling of the lesser saphenous and peroneal veins of the leg. Figure 4b was made immediately after Figure 4a and shows the normal femoral vein. Note that the profunda femoris is not visualized. Figure 4c is a view of the femoroiliac veins made immediately after Figure 4b.

This technique is far more reliable with the use of 70 per cent urokon than with previously available contrast media; however, filling the veins by this method lacks the obvious physiologic implications obtained by use of the proximal (penile vein) injection (Figs. 8, 9, and 10).

The vena cava may be visualized by exposure of a large (14 by 17 inch) film placed from the level of the sacrum to include the lower chest, with the x-ray exposure made immediately following rapid injection of the penile vein as previously described. A more reliable method for filling the vena cava is to place the patient on the large x-ray table with the head of the table elevated 15 degrees. Fifty cubic centimeters of 70 per cent urokon sodium are then injected into the dorsal vein in the ankle and fill the venous system of the lower extremity. After completion of the injection the ankle is grasped and the entire

a b

Fig. 7. Patient with left femoroiliac thrombosis. a, Left side fails to fill following injection of left lateral vein of penis. b, Thirteen days after Figure 7a. Injection of the left superficial circumflex iliac vein demonstrates collateral circulation. Another injection of the left lateral vein of the penis again failed to fill the left femoroiliac vein.

leg elevated 45 degrees so that the venous system is rapidly emptied into the vena cava. The x-ray exposure of the vena cava region is made within 10 seconds after elevation of the extremity. This insures a flow of the contrast medium from the great veins of the extremity into the vena cava during this period.

DISEASE PROCESSES DEMONSTRATED BY THE PROXIMAL INJECTION TECHNIQUE

Valvular incompetence. Incompetence of the valves of the venous system is characterized by: (1) filling of the entire femoral vein and veins of the lower leg when the patient is in a semierect position (Figs. 9 and 10) (filling of the veins of the lower leg may also occur by virtue of an incompetent greater saphenous vein); (2) dilatation and tortuosity of the veins (Fig. 10); (3) absence of the valvular cusp (Fig. 10); and (4) failure of the veins to empty themselves of contrast medium after muscular activity as described by Ferreira and associates.

Figure 8 illustrates filling of the veins of the thigh in a patient who was asymptomatic. No contrast material was found in the lower leg and this was considered to represent femoral incompetence of a minor degree.

Figure 9 illustrates more marked incompetence of the femoral veins of a patient who had symptoms of moderate venous incompetence. Figure 10 illustrates filling of the deep and superficial venous systems of the leg of a patient who had far advanced venous insufficiency secondary to thrombophlebitis with subsequent recanalization. Note the dilated and tortuous deep and superficial veins as well as the incompetent valves. Compare this with Figure 4 which illustrates a normal venogram of the lower leg obtained by injecting the lesser saphenous vein.

Chronic obstruction. Venous thrombosis in the early stages of recanalization produces the following characteristic findings on venography: (1) an irregular filling with tortuosity of the venous channel (Fig. 6b); (2) marked increase in the size and number of superficial veins (collateral circulation) which are not ordinarily visualized (Fig. 5c); and (3) reversal of blood flow in collateral circulation may be demonstrable (Figs. 5 and 6).

Figure 6a demonstrates the absence of filling of the left femoroiliac vein following in-

Fig. 8. Patient with relative incompetence of the left femoral vein. This patient had no symptoms.

Fig. 9. Patient with moderate incompetence of the deep veins of the right thigh.

ection of the median and lateral penile veins f the patient with clinical signs of acute hrombophlebitis. Figure 6b illustrates sev- ral small tortuous channels in the region of he left external iliac vein in the same patient 6 days after the onset of the symptoms of eep venous occlusion. This view is obtained y injection of the left lateral penile vein phlebothrombosis of the deep venous system as confirmed at an emergency abdominal peration for other reasons).

Acute venous obstruction. Venous throm- bosis and acute occlusion produced the fol- lowing characteristic findings on venography: (1) failure of the involved vein to fill with the contrast medium (Fig. 5a); (2) stasis of the dye in veins both distal and proximal to the point of obstruction (This is a reflection of the reduced rate of blood flow even in the veins which are patent proximal to the point of obstruction.); (3) marked increase in the size and number of superficial veins which are not ordinarily visualized, indicating the rapid development of collateral circulation (Fig. 5c); and (4) reversal of blood flow in collateral circulation sometimes demonstrable (Figs. 5 and 7) immediately after the signs and symptoms of deep venous occlusion develop.

Figure 7a illustrates occlusion of the deep venous system of the left leg in a patient with acute femoroiliac thrombosis. Figure 7b was made by injection of the superficial circum- flex iliac vein in the inguinal area and serves to demonstrate collateral circulation around the obstructed femoral and iliac veins by way of the superior gluteal veins

Figure 5a illustrates filling of the right femoral iliac system following injection of 50 cubic centimeters of 70 per cent urokon into the dorsal median superficial vein of the penis of a patient who had a left femoroiliac throm- bosis. Figure 5b demonstrates filling of the right femoroiliac system in the same patient following injection of a superficial tributary of the left greater saphenous vein. This is considered to represent reversal of blood flow in the left superficial pudendal vein. Figure 5c demonstrates filling of the superficial venous system of the left lower leg following injection of urokon sodium into the lesser saphenous system in the region of the lateral malleolus (compare with Fig. 4a). Figure 5d demonstrates filling of the superficial system of the left leg in the region of the thigh and pelvis with collateral circulation, carrying the contrast solution into the venous system of the right leg following injection of the same

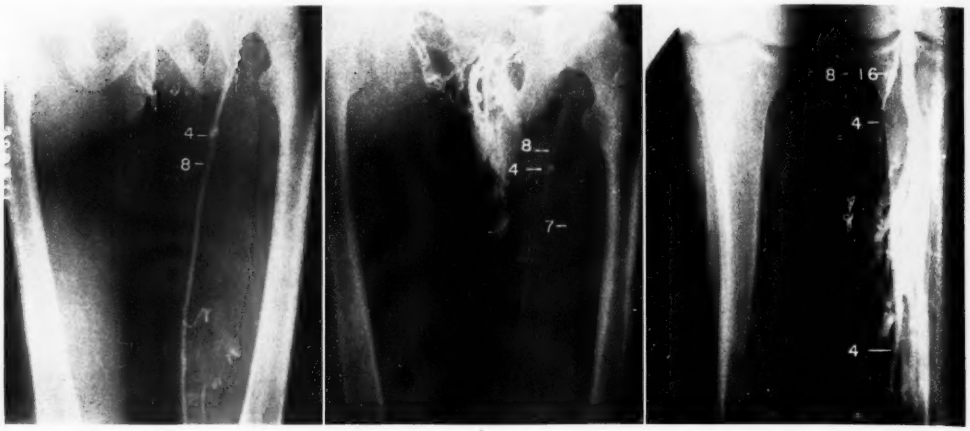

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Fig. 10. Incompetence of both the superficial and deep venous systems. a, The majority of the urokon has migrated down the incompetent greater saphenous vein. b, Digital pressure over the greater saphenous has diverted more of the urokon into the incompetent femoral vein. c, Roentgen exposure of the lower leg made immediately after Figure 10b. Note the absence of competent valves, the pooling of the urokon, and the free communications which are present between the deep and superficial venous systems.

vein of the ankle as Figure 5c (compare with Figs. 4b and 4c). This patient had complete occlusion of the deep venous system which did not fill by injection at any one of these several sites.

DISCUSSION

The advantages of venography of the pelvis and lower extremities as performed by the proximal injection technique are: (1) The technique is simple, requires no special equipment, local anesthesia, or physical exertion on the part of the patient and is, therefore, applicable even to the seriously ill patient. A single injection will suffice to demonstrate femoroiliac systems bilaterally in more than half the male individuals, and not more than 2 injections will be required in the remaining male or female patients. (2) Physiologic implications derived from the proximal injection technique are not available by any other method of venography. The contrast material will gravitate into the dependent veins to the point of the first competent valvular system. (3) The main trunk of the profunda femoris vein will be visualized by this technique, a feat which cannot be consistently duplicated by any method of distal injection. (4) There is the theoretical advantage that proximal instillation of the contrast medium will not affect the hemodynamics of the lower extremity in such a manner as to dislodge an embolus from an acute phlebothrombosis.

The indications for venography of the vena cava, the pelvis, and lower extremities are occasionally encountered in any medical practice. Bilateral venograms of the femoroiliac veins are important diagnostic studies in suspected venous thrombosis or pulmonary embolism of unknown origin. Venograms of the thigh and leg are desirable in the treatment of venous stasis and of value in the differentiation of venous and lymphatic obstruction in patients who have edema of obscure origin. Venography may be an important aid in establishment of competency of the superficial, deep, and communicating venous systems prior to surgical correction of venous stasis.

SUMMARY

A simplified technique which does not require anesthesia or special equipment has been described whereby bilateral roentgenographic visualization of the femoroiliac and leg veins and the vena cava may be obtained. The success of this technique is due largely to

the excellent contrast properties of buffered 70 per cent urokon sodium and to its relative high specific gravity as compared to whole blood. This physical property causes the dye to gravitate into the dependent venous system to the point of competent valves. The position of the patient is of greater importance in obtaining correct distribution than the quantity injected or the rate of administration.

It is not to be implied that venography of the proximal injection technique should supplant other methods of venography. Rather, each patient should be considered in the light of the clinical findings and a program of venography employed which will utilize one or more of the techniques to the best advantage for the individual. Seventy per cent urokon sodium has proved superior to any other available contrast medium by any technique.

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METASTASIZING BRONCHIAL ADENOMAS

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CONFLICTING opinions as to the life history of patients who have adenoma of the bronchus have led to some confusion as to the behavior of these neoplasms. As in all neoplasms, the treatment of adenoma of the bronchus must have for its rational basis as clear a concept as possible of the course of these tumors, the tendency for these tumors to metastasize, and their ultimate potentialities for killing.

This study of the cases of metastasizing adenomas of the bronchus, both carcinoid and cylindromatous in type, seen at the Mayo Clinic, together with a review of the literature was undertaken in order to focus attention on these concepts. It was hoped that an estimate could be made, from our own cases and from those recorded in the literature, of the incidence of metastasis in bronchial adenomas. Secondly, an attempt was made to elucidate the life history of metastasizing bronchial adenomas, using again data from these two groups of cases. Thirdly, a comparison of the histopathologic changes in metastasizing adenomas was made with those in nonmetastasizing adenomas.

REVIEW OF THE LITERATURE

Cases of metastasizing bronchial adenoma that have been reported in the literature may be divided into two groups. One group is that in which the cases are the subject of a special report replete with details and photomicrographs. The other group consists of those cases mentioned in discussions of papers or of cases in which evidence of metastasis was present and which were included in reports of series of nonmetastasizing bronchial adenomas. Some duplication may be present in these groups although we have attempted to eliminate this when possible. As this study is concerned only with those cases of bronchial adenoma in which metastasis has occurred distantly or to regional lymph nodes, our review of the literature includes only such cases. It was necessary, however, to review all the literature on bronchial adenoma to allow selection of this group.

It will be noted that in many cases in which invasion of the regional lymph nodes was present, evidence existed that this involvement was apparently by direct extension of the tumor into the node. Cases in which the regional nodes are involved by direct extension are thus included, although it is recognized that there may be some difference of opinion about these lesions being metastatic. Holley, Goldman, and others have noted occasional extension of adenomas into pulmonary vessels. In none of such cases did any evidence of distant metastasis exist. We have chosen not to include these cases as examples of metastasizing bronchial adenomas.

In the cases of Kirch, Malkwitz and Pein, reported in the early part of this century and which have been quoted by Graham and Womack as cases in which malignant transformation of adenomas took place, no evidence of any distant metastasis was noted; the lesions were called malignant on the basis of local infiltration in Pein's and Malkwitz's cases and because of the presence of mitotic figures and pleomorphism in Kirch's case. They are, therefore, omitted from this review. Baumgarten, in 1937, reported a case in which hepatic metastasis occurred but no details of the pathologic changes were included. This case also, therefore, is not included.

Heck, in 1916, was apparently the first to describe metastasis to lymph nodes in bronchial adenoma. Heck labeled his case as one of polypoid carcinoma but, as judged by the clinical and pathologic descriptions of the case and the tumor and the photomicro-

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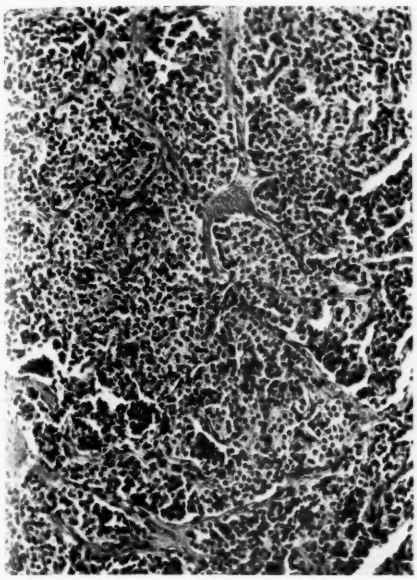

Fig. 1. Case 1. Primary tumor showing typical carcinoid pattern of bronchial adenoma; the cells are arranged in nests and cords with little tendency to glandular formation. Hematoxylin and eosin, ×110.

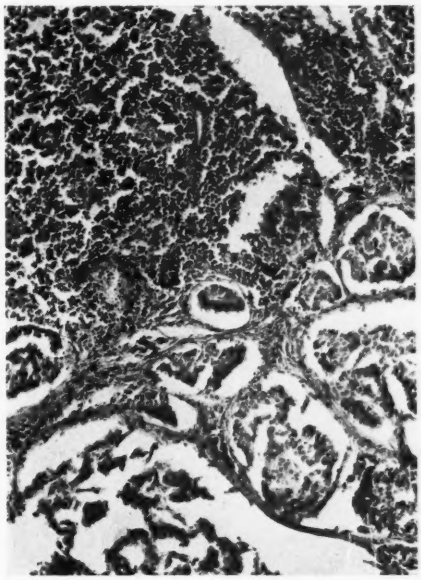

Fig. 2. Case 2. Involved lymph node adjacent to primary bronchial tumor; the cells are small, regular in size, and have a distinctly glandular pattern. Hematoxylin and eosin, ×101.

graphs, little doubt remains that the lesion in his case was an adenoma.

Since this first report, an increasing number of cases have been described in which a bronchial adenoma has metastasized to either lymph nodes or distant organs.

MATERIAL AND METHODS

All cases of bronchial adenomas, both carcinoid and cylindromatous in type, diagnosed and verified histologically at the Mayo Clinic from April, 1937, through January, 1952, were reviewed. Adenomas of the trachea were not included. This group of bronchial adenomas numbered 111; among these were found 9 cases of metastasizing adenomas. Of the total group of bronchial adenomas from the clinic, 86 have been reported previously; of the metastasizing adenomas, 4 have been reported previously.

Histopathologic changes in all tissues available in each of these cases were carefully studied. The case histories were reviewed and follow-up data were obtained.

REPORT OF CASES[1]

CASE 1. A 24 year old woman first registered at the clinic on October 8, 1940. She had had recurrent episodes of pneumonitis for the previous 2 years; an empyema had been drained the year before registration. A carcinoid type of adenoma was found in the left main bronchus; diathermy and implantation of radon seeds were used.

In 1948, a left pneumonectomy was done because of recurrence of the adenoma. A small amount of tumor was found in the left main bronchus and 3 regional lymph nodes were found to contain tumor. In February, 1952, 3 years and 5 months later, she reported that she was well.

The primary tumor (Fig. 1) was composed of small epithelial cells arranged in a carcinoid pattern throughout. Little or no pleomorphism and no mitotic figures were seen. The cytoplasm was scanty and eosinophilic. Sections of the 3 involved lymph nodes closely adjacent to the primary tumor displayed a similar carcinoid pattern; it was impossible to determine if this metastatic invasion was by direct extension or by embolism.

CASE 2. A 44 year old man entered the clinic on July 21, 1949, because of cough, malaise, and episodic fever of 5 years' duration. Bronchoscopic examina-

[1]Cases 1, 2, 3, and 9 have been reported previously by Moersch and McDonald.

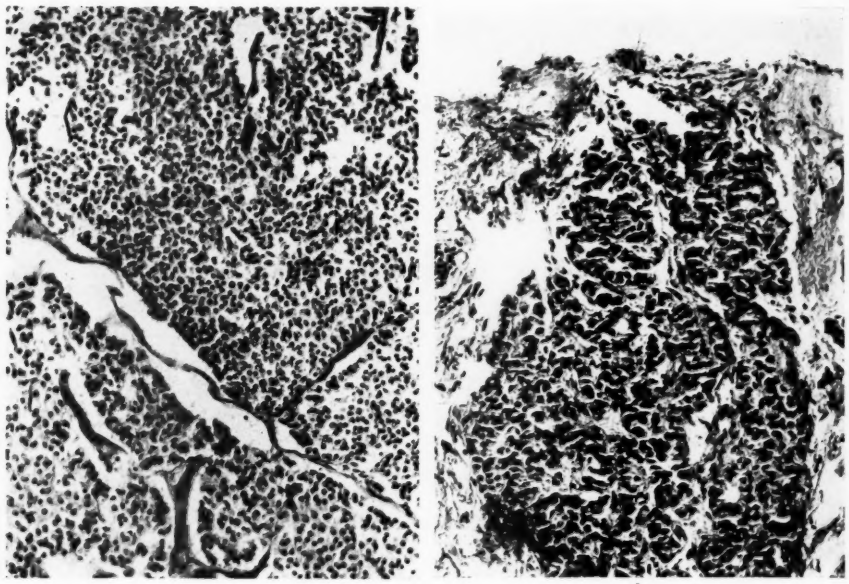

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Fig. 3. Case 3. a, Metastatic tumor in hilar lymph node; note small regular epithelial cells arranged in sheets. Hematoxylin and eosin, ×132. b, Metastatic lesion in liver showing nuclear irregularity, hyperchromatism, and pronounced acinar pattern. Hematoxylin and eosin, ×154.

tion revealed a tumor in the bronchus of the upper lobe of the right lung.

A right pneumonectomy was done on August 4, 1949. A polypoid tumor 1.2 by 1 by 0.8 centimeter was found in the bronchus. One lymph node immediately adjacent to the tumor was found to be invaded. In February, 1952, 2 years and 5 months later, he reported that he was well.

Histologically, the tumor was a typical bronchial adenoma of the carcinoid pattern. It was composed of small epithelial cells that were regular in size and arranged in cords and acini. No mitotic figures were noted. The lymph node appeared to be involved by direct extension (Fig. 2).

CASE 3. A 49 year old man was first seen at the clinic on October 2, 1936, because of hemoptysis, cough, and episodes of pneumonitis for 1 month. A carcinoid type of adenoma was found in the right main bronchus. During the ensuing 10 years, he had 14 endoscopic treatments with diathermy and radon seeds.

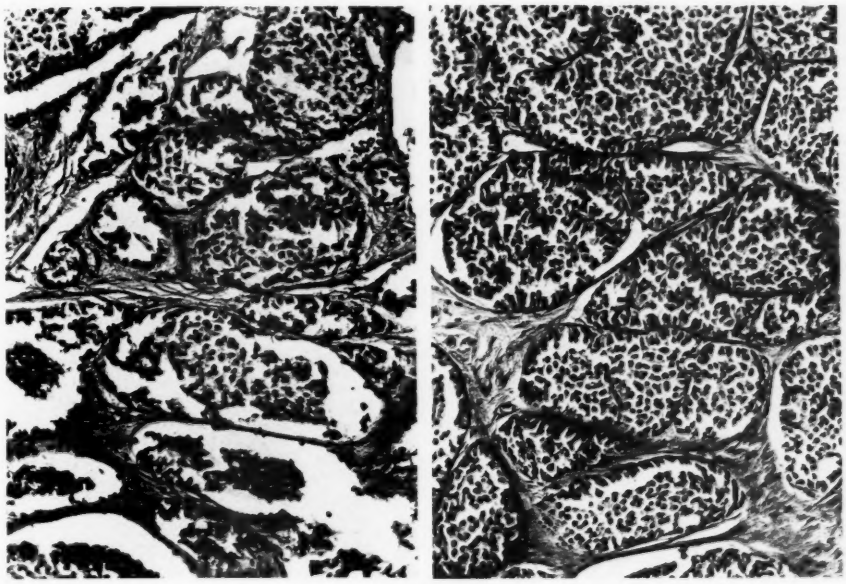
In January, 1946, a right pneumonectomy was done. A tumor 1.5 centimeters in diameter was found in the bronchus of the lower lobe; 4 regional nodes were metastatically involved. Empyema developed postoperatively and was successfully treated by open drainage.

The patient returned in July, 1948; at this time, evidence of spinal and hepatic metastatic lesions was present. Abdominal exploration revealed metastasis to the liver. The patient died 6 months later, 3 years after the pulmonary resection and 13 years after the tumor was first diagnosed.

Histologic section of the primary tumor and metastatically involved lymph nodes (Fig. 3a) showed small regular cells arranged in broad sheets separated by a delicate stroma of connective tissue. A slight tendency to acinar formation was noted but this was much less pronounced than in Case 2. No mitotic figures or areas of necrosis were found. The tumor was classified histologically as a metastasizing bronchial adenoma. Biopsy of the liver (Fig. 3b) suggested an increase in malignancy of the tumor in that the nuclei were somewhat larger, showed much more variation in size and shape and were deeply hyperchromatic. The tendency to acinar formation was much greater than in the primary lesion.

CASE 4. A 53 year old woman came to the clinic on June 13, 1949, because of an 8 year history of recurrent pneumonitis. A large adenoma of the carcinoid type was found in the right bronchus intermedius; a right pneumonectomy was done. Examination of the specimen revealed a tumor, 4.5 centimeters in diameter, in the right main bronchus and bronchus intermedius. Many regional nodes were invaded.

She did well postoperatively until 10 months later when she noted a lump beneath the skin along the



a b

Fig. 4. Case 4. a, Primary carcinoid adenoma of bronchus; the cells are somewhat larger than those of the preceding tumors. b, Metastatic lesion in skin of thoracic wall showing a similar pattern, with maintenance of carcinoid structure. Both hematoxylin and eosin, ×110.

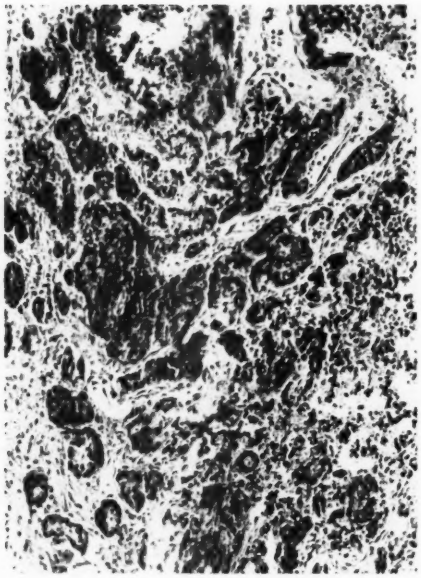
er border of the left pectoralis major muscle. Biopsy revealed a tumor that was identical with that found in the lung. A year and 4 months later 2 lumps appeared, 1 on the back of her neck and 1 beneath the skin over the abdomen. These were removed; the microscopic appearance again was identical with that of the pulmonary tumor. Follow-up in August, 1952, revealed that she had multiple subcutaneous nodules and felt ill most of the time.

Microscopic examination of the primary tumor revealed a bronchial adenoma of carcinoid type (Fig. 4a). The cells were grouped in large masses separated by delicate septa of connective tissue. They were slightly larger in size than cells noted in the usual bronchial carcinoid and were oval, cuboidal, or columnar in shape. A moderate amount of eosinophilic cytoplasm was present. The nuclei were regular and somewhat hyperchromatic and displayed a single rather prominent central nucleolus. An acinar pattern was noted in some areas. The metastatically involved lymph nodes and the metastatic nodule from the skin disclosed a similar histologic picture (Fig. 4b). A more pronounced fibrous reaction was present in the cutaneous lesion and mitotic figures, while not numerous, could be found without prolonged search.

CASE 5. A 36 year old man first registered at the clinic on February 15, 1949. One year previously he had had a right lower lobectomy for a "malignant adenoma with regional nodal involvement." He had noted symptoms of hemoptysis and pneumonitis for about 2 years prior to his operation. He came to the clinic because of symptoms of hyperparathyroidism. On March 12, 1949, resection of the parathyroids was done. In a cervical lymph node in the region of one of the parathyroid glands was an area in which a small-celled neoplasm was present; this was apparently metastatic from the bronchial tumor. Roentgen ray therapy was given.

The patient returned November 20, 1950, at which time biopsy of a mass in the neck disclosed a tumor that was identical with the metastatic lesion in the cervical lymph node. More roentgen ray therapy was given and the cervical mass disappeared. The patient returned in January, 1952, at which time a small subcutaneous mass of identical histologic appearance was removed from the thoracic wall. In June, 1952, he was again seen and multiple metastatic lesions in the bones were found. Roentgen ray therapy was again given with some benefit. He was again seen in September, 1952, and further radiation treatment advised because of metastasis to the skull.

Sections of the primary tumor and regional lymph nodes revealed a bronchial adenoma of carcinoid type. The cells were small and regular and no mitotic figures were evident. A pronounced adenomatoid pattern was present in parts of the primary



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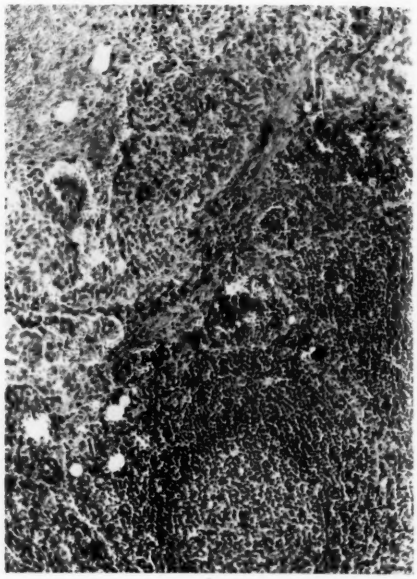

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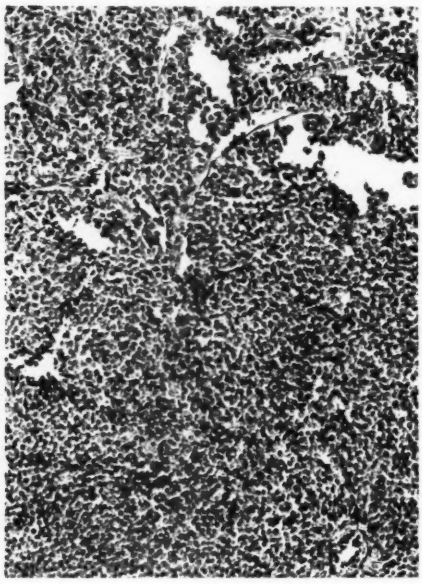

c

Fig. 5. Case 5. a, Primary bronchial tumor showing an area with marked acinar arrangement. b, Metastatic lesion in the hilar node showing well organized carcinoid tumor. c, Metastatic lesion in skin of thoracic wall showing sheets of small cells without any structural pattern; mitotic figures are present. All hematoxylin and eosin, ×132.

tumor (Fig. 5a) but this was less prominent in the nodal metastatic lesions (Fig. 5b). The metastatic lesions in the cervical region and in the skin of the thoracic wall (Fig. 5c) revealed a considerably more undifferentiated appearance. No attempt at acinar formation was present, the cells being arranged in broad sheets. Mitotic figures, although not numerous, were found without prolonged search.

CASE 6. A 44 year old woman registered at the clinic on February 6, 1950, because of a 7 month history of cough and thoracic pain. A roentgenogram of the thorax taken 9 months previously showed nothing abnormal. A polypoid tumor was found that obstructed the bronchus of the middle lobe of the right lung. General examination revealed a small adnexal mass and small nodule in abdominal wall.

Total abdominal hysterectomy and bilateral oophorectomy and salpingectomy were done in February, 1950; the nodule in the abdominal wall was excised. The ovaries and the nodule from the abdominal wall revealed metastatic tumors microscopically suggestive of bronchial adenoma. One month later, thoracic exploration revealed a large hilar mass with many involved nodes and evidence of mediastinal extension. Biopsy of an invaded node was carried out. The patient died 7 months later.

The primary tumor in the bronchus consisted of small hyperchromatic epithelial cells arranged in nests, strands, and poorly formed acini; a moderate amount of connective tissue stroma was present. Mitotic figures were rare. Some irregularity of the

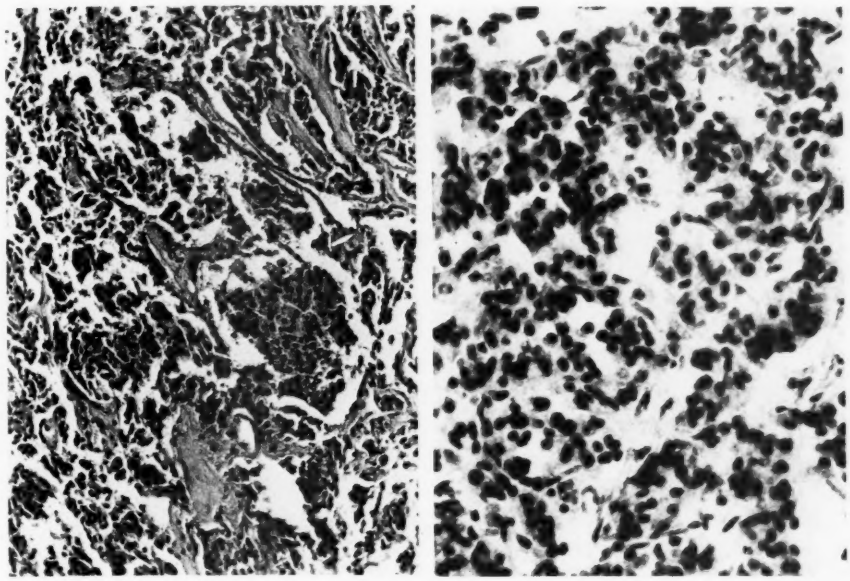

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Fig. 6. Case 6. a, Primary tumor of bronchus. The appearance under low power suggests a bronchial carcinoid but considerable disorganization of architecture is present. Hematoxylin and eosin, ×110. b, Metastatic lesion in ovary showing cells at higher magnification. Hematoxylin and eosin, ×309.

nuclei was noted and the pattern was obviously more disorderly than that seen in the usual bronchial carcinoid (Fig. 6a). Metastasis to the ovary (Fig. 6b) and abdominal wall exhibited a similar atypical carcinoid pattern.

CASE 7. A 55 year old woman entered the clinic on January 7, 1952, because of a 6 month history of thoracic pain and recurrent pneumonia. A tumor was found in the right bronchus intermedius. The microscopic appearance was that of a bronchial adenoma of atypical pattern. Thoracic exploration in February, 1952, disclosed an inoperable tumor that had invaded many lymph nodes. Biopsy of the nodes was obtained and roentgen ray therapy was given postoperatively. She returned in September, 1952, at which time she felt well; the roentgenographic shadow of the pulmonary tumor had almost entirely disappeared. No evidence of distant metastasis was present.

Histologic examination of the primary bronchial tumor (Fig. 7a) revealed a small cell neoplasm with regular nuclei arranged in sheets; a tendency toward poorly formed acini was noted. No mitotic figures were found. Examination of the mediastinal lymph nodes (Fig. 7b) revealed a similar histologic pattern; a slightly decreased tendency to acinar formation was noted.

CASE 8. A 37 year old man came to the clinic on May 7, 1943, because of a 3 year history of hemoptysis and recurrent pneumonitis. A carcinoid type of adenoma was found in the right main bronchus and right pneumonectomy was done in June, 1943. A tumor measuring 5 by 2 by 1.5 centimeters was found in the middle lobe.

He did well postoperatively but 3 years later returned because of pain in the left leg and hip. A metastatic lesion was demonstrated roentgenographically in the left femur and roentgen ray treatment was given. Four years later, he returned complaining of pain in the left hip. The metastatic lesion was biopsied. The patient died 5 months later.

The primary bronchial tumor (Fig. 8a) was composed of small epithelial cells that showed a tendency to glandular formation in some regions. The nuclei were more hyperchromatic than those noted in the usual bronchial carcinoid and rare mitotic figures were found. The pattern was disorganized. The metastatic nodule in the femur (Fig. 8b) was similar in appearance but displayed a slightly more pronounced acinar structure.

CASE 9. A 69 year old man entered the clinic in June, 1947, because of a 1 year history of weakness, thoracic pain, and productive cough. A carcinoid type of adenoma was found in the upper lobe of the left lung. The patient was treated endoscopically 4 times in the next year. The liver was found to be enlarged at this time and hepatic biopsy was done. This revealed tissue identical with that in the lung.

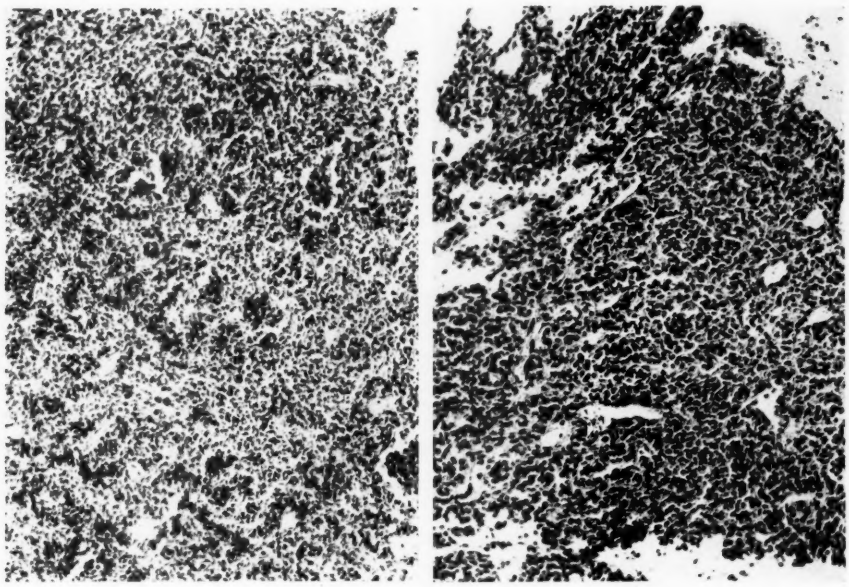

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Fig. 7. Case 7. a, Primary tumor; in spite of increased cellularity, some tendency to form acini is present. Hematoxylin and eosin, ×110. b, Metastatic lesion in mediastinal lymph nodes showing little or no organization. Hematoxylin and eosin, ×132.

He continued to do fairly well. Bronchoscopy was again done 1 year after the hepatic biopsy. The patient died 2 years and 3 months after he was first seen at the clinic.

Histologic section of the bronchial tissue removed at biopsy in 1947 (Fig. 9a) revealed a bronchial adenoma composed of small epithelial cells with regular nuclei. No mitotic figures were seen. The cells were arranged in ribbons, nests, and fairly well formed acini. Abundant fibrous stroma was present. The metastatic lesion in the liver (Fig. 9b) was essentially similar in appearance.

RESULTS

Incidence. In our group of 111 cases of bronchial adenomas, 9 metastasizing adenomas were found, an incidence of 8.1 per cent. Through July, 1952, there have been reported in the literature approximately 700 cases of adenoma of the bronchus, excluding those cases reported from this institution; of these, 78 were metastasizing adenomas. This study has, therefore, disclosed a total of 87 such cases. It would thus appear that metastasis occurs in approximately 10 per cent of bronchial adenomas.

Histopathologic aspects. In our own group of cases, several facts became apparent from a study of the pathologic material.

In those cases in which metastasis was to nodes only (Cases 1 and 2), the histologic appearance was typical in every respect of the classic carcinoid type of bronchial adenoma, namely, the cells were uniform, had small regular nuclei, and were arranged in a pattern suggestive of the carcinoid tumors seen in the intestine. No mitotic figures and no significant pleomorphism were noted in these lesions.

In Case 3, in which regional and distant metastasis occurred, the primary tumor and the metastatic foci in adjacent lymph nodes presented a fairly typical carcinoid appearance (Fig. 3a). The histologic picture of the hepatic metastatic lesions was highly atypical and showed nuclear irregularity and obvious hyperchromatism. In general, the microscopic appearance suggested a definite increase in malignancy on the part of the tumor.

In Case 4, in which regional and distant metastasis was also present, the cells ap-

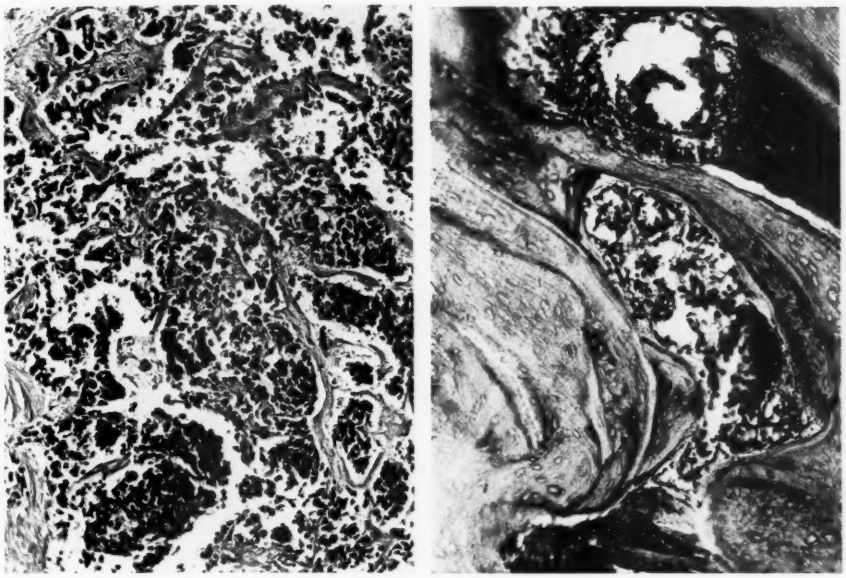

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Fig. 8. Case 8. a, Primary lesion. b, Metastatic lesion in femur. Both hematoxylin and eosin, ×110.

ured slightly larger and the nuclei more hyperchromic than those of typical bronchial adenomas of the carcinoid type. Infrequent mitotic figures could be found in both primary and distant metastatic lesions. Both primary and distant metastatic lesions were identical in histologic structure and, in general, aside from the slight departures from usual just mentioned, the carcinoid appearance and pattern were well preserved.

In Case 5, the primary lesion and the metastatic lesions in the regional lymph nodes presented an orderly carcinoid appearance with definite acinar pattern in some parts, as shown in Figure 5a and b. The metastatic lesions in the cervical lymph node and the skin of the neck (Fig. 5c) showed a more undifferentiated picture in that the cells contained less cytoplasm, mitotic figures were found without difficulty and complete absence of organization was present. In spite of these changes, the histologic picture was not nearly so undifferentiated as that seen in small cell bronchogenic carcinoma.

The tumors in Cases 6, 7, and 8 all had an atypical histologic appearance; the cells exhibited some pleomorphism, occasional mitotic figures and lack of the typical carcinoid pattern. In all 3 cases, however, sufficient histologic evidence of bronchial adenoma occurred to compel their inclusion in this group. The gross appearance and clinical behavior of the tumors in these 3 cases gave added support to the diagnosis.

In Case 9, in which distant metastasis occurred, the histologic pattern was more orderly and presented a similar pathologic picture in both the primary tumor and the hepatic metastatic lesions.

Although it is difficult to evaluate the histopathologic changes in the cases reported in the literature, it appears that, in general, the reported cases parallel those in our series in many respects. Most tumors that had an orderly carcinoid pattern did not metastasize distantly, whereas in most tumors that did, the presence of atypical features, such as pleomorphism, mitotic figures, and irregular cellular pattern, was noted in the metastatic lesions or the primary tumor or both.

The statement has been made many times that lesions presenting the cylindromatous

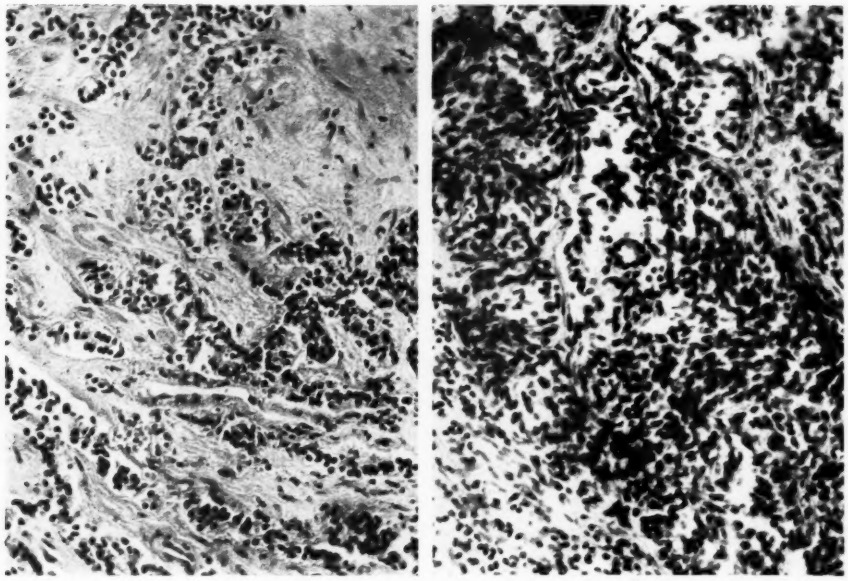

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Fig. 9. Case 9. a, Primary bronchial tumor showing fairly typical carcinoid pattern. b, Hepatic metastatic lesion showing well organized acinar pattern. Both hematoxylin and eosin, ×193.

pattern are more malignant than those exhibiting the carcinoid structure (3). In the 87 cases with which this review is concerned, 52 tumors were included in which the cellular pattern was described or in which the pattern was not stated but the photomicrographs were of sufficiently good quality to allow one to draw some conclusion in this regard. Of these 52 tumors, 38 were of the carcinoid type and 14 were of the cylindromatous type. Of our own 9 cases, all were of the carcinoid type. Thus, on the basis of cases reported in the literature, it appears that roughly 3 times as many instances of metastasis occurred in tumors of carcinoid pattern than in tumors of cylindromatous pattern; however, if it is recalled that adenomas of the cylindromatous type make up only about 10 per cent of the entire group, it appears that metastasis is approximately 3 times as apt to occur in tumors of cylindromatous pattern than it is in those of the carcinoid type.

Life history of patients who have metastasizing adenomas. Of our 9 patients who had metastasizing bronchial adenomas, 6 had invasion only of the lymph nodes within the thorax at the time of their first operation. Two of the 9 patients had distant metastasis when first seen, while the remaining patient had no metastasis either nodal or distant when first examined but later experienced distant metastasis.

Of the 6 patients who had involvement only of the nodes when first seen, 1 was inoperable because of the massiveness of this nodal invasion. Distant metastasis later developed in 3 of the patients; the other 2 have not experienced distant metastasis to date. It is of interest that the 2 patients in whom later trouble has not developed are those in whom the nodal metastasis was apparently by direct extension.

Of the total group of 9 patients then, distant metastasis has developed in 6. Three of these originally had only nodal metastasis as noted above and 2 had distant metastasis when first seen; no metastasis was noted in 1 patient when first seen but distant metastasis later developed. Of this group of 6 patients who had distant metastasis, 4 are dead of the

metastatic disease; the remaining 2 are failing rapidly and little hope can be held for their prolonged survival. It is evident from our study, however, that a patient may live for several years even with definite distant metastatic disease.

Study of the cases reported in the literature permits little in the way of prognostic evaluation. It appears, however, that these cases generally parallel our own cases in that when lymph nodes only are involved, particularly by direct extension, the prognosis is relatively good and when distant metastasis has occurred prognosis is poor but survival may be prolonged for many months or even years before death ensues. Of especial interest is the case of Gordon, in which a metastatic lesion was removed from the liver 5 years after the pulmonary tumor had been resected; the patient was still living and working when the case was subsequently reported, although the length of time that had elapsed was not given.

Site of metastasis. Of the 87 cases in the literature, including ours, 46 presented evidence of regional nodal metastasis only. In all of this latter group of cases, it was stated that nodal involvement was by direct extension. This was implied but not so stated in several others.

In the other cases, 41 in number, metastasis was present in the following organs in decreasing order of frequency: (1) liver, (2) opposite lung, (3) ipsilateral lung, (4) pleura, (5) esophagus and other mediastinal structures, (6) bone, and (7) miscellaneous organs, including brain, kidney, and adrenal gland.

COMMENT

As previously indicated, the treatment of all neoplasms must depend on an understanding of their life history. Evidence exists that a significant number of bronchial adenomas, probably about 10 per cent, metastasize to either the regional lymph nodes or distant organs. It is also known that obstructive pneumonitis with suppuration complicates bronchial adenomas in a significant number of cases (10). In view of these facts, it is probable that pulmonary resection of as conservative a nature as is possible constitutes the treatment of choice for patients who have bronchial adenoma. A more radical resection is justified if any evidence of metastasis is found at operation or if the results of biopsy make it evident that the adenoma may have metastasizing potentialities. This judgment must be tempered by the realization that cases still occur in which endoscopic removal and close follow-up may be justified.

SUMMARY

A review of the literature concerning bronchial adenomas, together with a study of cases involving such tumors at the Mayo Clinic has yielded 87 instances of bronchial adenoma in which metastasis occurred. Nine of these cases were encountered at the clinic. This study demonstrated that metastasis takes place in approximately 10 per cent of all bronchial adenomas.

The histopathologic picture may in some cases indicate that the tumor in question may have metastasizing potentialities. None of the bronchial adenomas in our series that had a perfectly regular carcinoid pattern and little or no pleomorphism or mitotic figures metastasized distantly; in 2 cases, however, such adenomas did metastasize to lymph nodes. In those tumors that metastasized distantly, the carcinoid pattern was not orderly, and in 1 lesion no evidence of either carcinoid or cylindromatous pattern was present. Pleomorphism, mitotic figures, and irregularity of cellular pattern were more frequent in those adenomas that did metastasize distantly. It appears that adenomas of the cylindromatous type are 3 times as likely to metastasize as are adenomas of the carcinoid type; the importance of this tendency is lessened by the fact that only about 10 per cent of bronchial adenomas are of the cylindromatous type.

The patient who has bronchial adenoma may live several years even with definite distant metastasis. Except under special circumstances, patients who have bronchial adenoma are best treated by appropriate pulmonary resection.

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THE METABOLISM OF FRESH, TRANSPLANTED, AND PRESERVED CARTILAGE

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REPORTS concerning the viability of cartilage grafts have been based primarily upon gross observations and the interpretation of static histologic data. There is no information in regard to the metabolic activity of these transplants. This study was, therefore, undertaken to compare manometrically two phases of carbohydrate metabolism (respiration and anaerobic glycolysis) in fresh costal cartilage with that of preserved cartilage, cartilage autografts, and fresh and preserved homografts. These metabolic processes represent the important energy source of all cells and are thus intimately related to tissue viability.

MATERIAL

One hundred and sixty nonlittermate, female albino rabbits, approximately 3 months of age and 2 kilograms in weight, were utilized as donors and recipients of costal cartilage. Four types of transplants were studied. The first group consisted of 53 costal cartilage grafts which were implanted in the abdominal wall of the donor animals (autografts). The second group was made up of 53 grafts taken from the donors and directly transplanted to other rabbits (direct homografts) (Fig. 1). In the third group of 49 grafts, the cartilage was first preserved for 7 days by rapid freezing and dehydration before being transferred to the recipient animals (indirect homografts, frozen-dried). The fourth group consisted of 10 cartilage grafts which were preserved in merthosaline for 7 days prior to implantation (indirect homografts, merthosaline).

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The transplants in the first three groups were removed for manometric study at intervals of 7, 11, 15, 30, 60, 90, 120, and 150 days after implantation. Those which had been previously preserved in merthosaline were removed after 7 days. Determinations of respiration and anaerobic glycolysis were also made upon 20 specimens of costal cartilage immediately following their excision from donor animals of similar age and weight as those used for the grafts. These served for the comparison of the metabolism of fresh and transplanted tissue. In addition, the metabolic activity of 20 specimens of nontransplanted cartilage frozen-dried for 7 and 84 days, and 40 of cartilage preserved in merthosaline for periods of 7, 21, 28, and 91 days were studied. As a further control, 6 samples of fresh cartilage were analyzed after being autoclaved for 30 minutes at 255 degrees F. with 20 pounds of pressure.

SURGICAL PROCEDURE

Each rabbit was anesthetized by an injection of 0.5 cubic centimeter of a 3 per cent solution of sodium pentobarbital per kilogram of body weight into the marginal vein of the ear. All cartilage specimens, whether for implantation or preservation, were utilized devoid of perichondrium. For the autografts, the left sixth and seventh costal cartilages were removed and immediately implanted subcutaneously in the abdominal wall. Each piece measured approximately 3 millimeters in diameter and 3 centimeters in length. For the homografts, the fourth, fifth, sixth, and seventh costal cartilages were excised bilaterally. In the direct homografts, 2 pieces of cartilage were immediately implanted subcutaneously in each of 4 quadrants of the abdominal wall of the recipient animals. In the indirect homografts, the surgical procedure was similar, with variations

TABLE I.—COMPARISON OF RESPIRATION AND ANAEROBIC GLYCOLYSIS OF FRESH, TRANSPLANTED, PRESERVED, AND AUTOCLAVED RABBIT COSTAL CARTILAGE

Costal cartilage	Days of implantation or storage	No. of specimens	Mean rate respiration	No. of specimens	Mean rate anaerobic glycolysis
Fresh	.....	10	−0.41±0.04	10	+0.70±0.08
Autograft*	7–150	25	−0.23±0.08	28	+0.46±0.12
Direct homograft*	7–150	28	−0.22±0.07	25	+0.40±0.13
Frozen-dried homograft	7–150	25	−0.07±0.03	24	+0.14±0.08
Merthosaline homograft	7	5	−0.09±0.01	5	+0.12±0.01
Frozen-dried Preserved	7	5	−0.07±0.01	5	+0.11±0.01
	84	5	0	5	+0.13±0.02
Merthosaline Preserved	7–28	15	−0.07±0.02	15	+0.03±0.02
	91	5	0	5	0
Autoclaved	....	3	0	3	0

*The mean rates of respiration and anaerobic glycolysis for the autografts and homografts differed from the values of fresh cartilage at less than the 1 per cent level of probability.

only in the method and period of tissue preservation prior to transplantation.

METHODS OF PRESERVATION

Frozen-dried cartilage. Directly following removal from the donor animals, the cartilage was frozen by placing it in a beaker containing isopentane which was kept at −150 degrees C. by immersion in liquid nitrogen. The cartilage was then transferred to a sterile container and inserted rapidly into a modified Altmann-Gersh freezing-drying apparatus (4). The temperature was maintained at approximately −38 degrees C. After 7 days, a portion of the cartilage was removed from the unit and allowed to reach room temperature. Some of this tissue was immediately analyzed for metabolic activity. The rest was implanted in the recipient rabbits where it was rehydrated by the tissue fluids. The remaining cartilage was kept in the freezing-drying apparatus for 84 days prior to analysis.

Merthosaline cartilage. Following excision from the donor rabbits, the cartilage was placed in a solution containing 1 part of aqueous merthiolate (1:1,000) and 4 parts of normal saline and refrigerated at 5 degrees C. for 7 days. At the end of this time, the cartilage was rinsed in normal saline and implanted in the same manner as the other homografts. Samples of similarly preserved nontransplanted cartilage were stored for 7, 14, and 28 days before being studied. A group of specimens was also kept for 91 days, but during this period the merthosaline solution was changed 8 times at varying intervals.

METABOLIC ANALYSIS

After the specified period of implantation, the grafts were excised, carefully stripped of soft tissues, and then immediately sliced in cross-section to a thickness of 0.3 millimeter by means of a modified microtome. An average of 250 milligrams of sliced cartilage was placed in each Warburg flask. The nonimplanted frozen-dried and merthosaline preserved specimens were similarly prepared.

Respiration and anaerobic glycolysis were studied by the standard manometric methods. The suspending medium for the tissue slices in the aerobic determinations consisted of 2.0 milliliters of Krebs-Ringer phosphate solution *p*H 7.4 and 0.2 milliliter of a 10 per cent glucose solution. In addition, since the normal oxygen uptake of cartilage was very small, 0.2 milliliter of 0.001 molar aqueous methylene blue was added to increase the rate of respiration to a more accurately measurable level. Into the center well of each flask, 0.2 milliliter of a 2 normal potassium hydroxide solution together with a small piece of fluted filter paper was placed for the absorption of carbon dioxide. The manometers were gassed for 10 minutes with pure oxygen bubbled through water.

The suspending medium for the anaerobic investigations consisted of 2.0 milliliters of Krebs-Ringer bicarbonate solution, 0.4 milliliter of distilled water, and 0.2 milliliter of 10 per cent glucose. The manometers were gassed with a water saturated mixture of 95 per cent nitrogen and 5 per cent carbon dioxide.

The flasks were placed in a constant temperature water bath maintained at 38 degrees C. and oscillated approximately 120 times a minute. The manometers were allowed to equilibrate for 15 minutes, readings

then being taken at 15 minute intervals over a 2 hour period. Respiration (QO_2) and anaerobic glycolysis ($Q_G^N{}_2$) were expressed as microliters per hour per milligram of dry tissue.

RESULTS

Fresh costal cartilage. The results obtained from the study of the respiration and anaerobic glycolysis of fresh costal cartilage appear in Table I. In 20 determinations with cartilage from different rabbits, the mean QO_2 (microliters of oxygen taken up by 1 milligram dry weight of cartilage per hour) was found to be -0.41 ± 0.04, while the $Q_G^N{}_2$ figure (microliters of CO_2 equivalent to the acid produced by 1 milligram dry weight of cartilage per hour under anaerobic conditions) was $+0.70 \pm 0.08$. No metabolic activity was recorded from the autoclaved specimens. This series of experiments comprised the group with which the values obtained from the transplanted and nontransplanted preserved cartilage were compared.

Transplanted cartilage (direct and indirect). For the study of the metabolism of transplanted cartilage generally not less than 3 grafts were tested at each of the specified time periods. After implantation for 7 days, the mean rates of respiration and anaerobic glycolysis for the autografts, and the direct and frozen-dried homografts were -0.26, -0.32, and -0.06 respectively. For the periods from 7 to 150 days (11, 15, 30, 60, 90, 120 days) after transplantation the mean QO_2 values for the autografts varied between -0.13 and -0.29. In the direct homografts the rates ranged from -0.16 to -0.28, while in the frozen-dried homografts they varied between -0.03 and -0.09. The merthosaline homografts were studied only after a 7 day implantation period. The mean QO_2 was -0.09 at the end of that time.

The mean $Q_G^N{}_2$ values were consistently higher than the corresponding QO_2 figures. After the 7 day implantation period, the mean rates of anaerobic glycolysis for the autogenous, direct, and frozen-dried homogenous grafts were $+0.50$, $+0.54$, and $+0.07$ respectively. For the interval from 7 to 150 days the values varied from $+0.34$ to $+0.57$ in the autografts, $+0.29$ to $+0.50$ in the direct homografts, and $+0.02$ to $+0.26$ in the frozen-dried transplants. The mean $Q_G^N{}_2$ figure for the 7 day merthosaline homografts was $+0.12$.

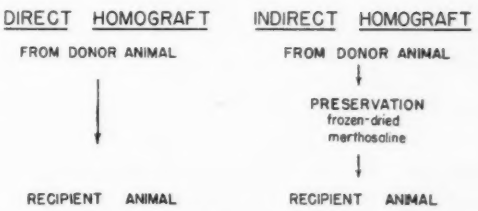

Fig. 1. Types of cartilage homografts. The donor and recipient are different individuals of the same species.

Preserved cartilage. The mean values for the respiration and anaerobic glycolysis of 10 samples of nontransplanted cartilage which had been preserved in the freezing-drying apparatus for 7 days were -0.07 ± 0.01 and $+0.11 \pm 0.01$ respectively. After 84 days the mean $Q_G^N{}_2$ value for 5 specimens was $+0.13 \pm 0.02$, but respiratory activity could no longer be recorded.

The mean QO_2 figure for the merthosaline preserved cartilage was -0.06 ± 0.02 at the end of 7 days, -0.08 ± 0.02 at 21 days, and -0.07 ± 0.02 after 28 days. The $Q_G^N{}_2$ values for similar periods were $+0.03 \pm 0.02$, $+0.02 \pm 0.01$, and $+0.04 \pm 0.02$. No metabolic activity was found in the 91 day samples. Ten specimens were analyzed at each interval.

DISCUSSION

The metabolism of fresh costal cartilage. With the exception of a note on the metabolism of fresh rat costal cartilage (2), previous metabolic investigations have been limited primarily to fresh articular cartilage. These studies revealed that the rate of respiration and anaerobic glycolysis of cartilage is among the lowest of all tissues (Table II). The results from this investigation of fresh costal

TABLE II.—VALUES FOR RESPIRATION AND ANAEROBIC GLYCOLYSIS OF VARIOUS TISSUES OF THE RAT

Tissue	Respiration	Anaerobic glycolysis
Kidney (5)	−21.0	+3.0
Retina (5)	−19.0	+88.0
Liver (7)	−13.2	+3.3
Brain (5)	−13.0	+19.0
Thyroid gland (5)	−13.0	+2.0
Intestinal mucosa (5)	−12.0	+4.0
Spleen (5)	−12.0	+8.0
Salivary gland (7)	−9.0 to −24.0	+3.3 to +6.9
Cornea (rabbit) (3)	−1.56	+2.32
Costal cartilage (2)	−0.45	+1.6

cartilage compared favorably with these earlier findings.

The relative acellularity of cartilage is partially responsible for its low rate of metabolism. Bywaters, however, demonstrated that when cell counts were considered, the glycolytic activity per cell was similar to that of most other tissues. The rate of respiration per cell, on the other hand, was between 1/50 and 1/100 of that of other tissues. This seems to signify that the metabolism of cartilage is predominately anaerobic.

The effect of preservation upon the metabolism of cartilage. After preservation for 7 days in the freezing-drying apparatus, the cartilage exhibited very little metabolic activity (Table I). By the eighty-fourth day, oxygen consumption could no longer be recorded, but the rate of anaerobic glycolysis had shown no further decline. This would seem to indicate that the rapid freezing and dehydration process has an adverse effect upon certain of the enzymes involved in the degradation of carbohydrates, especially those concerned with respiration. It has been demonstrated that some of the more labile enzymes such as the dehydrogenases may fail to survive prolonged exposure to freezing temperatures. Studies on the effect of freezing-drying upon tissues, moreover, have shown that a considerable reduction occurs in succinoxidase and cytochrome oxidase activity. An involvement of only a single enzyme in each phase of carbohydrate metabolism would be sufficient to produce the observed changes.

The costal cartilage preserved in merthosaline also showed a marked decrease in respiration and anaerobic glycolysis at the end of 7 days. This result could probably be attributed to the action of the mercury present in the merthosaline solution. Mercury is capable of forming complexes with sulfhydryl groups (−SH) contained in many of the cellular enzymes and can thus inhibit their activity. Enzymes essential for the metabolism of carbohydrates such as succinic dehydrogenase, phosphoglucomutase, and triosephosphate dehydrogenase, among others, contain these groups.

Storage in merthosaline for 21 and 28 days failed to bring about any further significant alterations in respiration and anaerobic glycolysis beyond those observed after 7 days. All these data were, therefore, considered collectively (Table I). The cartilage that was subjected to repeated changes of solution, however, showed a complete absence of carbohydrate metabolism when analyzed. This resulted from bringing the unaffected enzymes in contact with additional quantities of mercury. Since the preparation and storage of such cartilage for clinical use entail frequent solution changes, it is very likely that most merthosaline preserved homografts are devoid of enzymatic activity at the time of implantation.

The fact that cartilage metabolism was not immediately abolished by either freezing-drying or storage in merthosaline does not necessarily imply the presence of viable chondrocytes. More likely, the recorded values were the result of the function of enzymes that were not inhibited or destroyed during the preservation period. The fact that some anaerobic metabolism could be shown in the 84 day frozen-dried specimens, while respiration was completely absent, seems to confirm this point. Further evidence is derived from the demonstration of complete metabolic suppression in the merthosaline preserved cartilage only after exposure to additional concentrations of mercury by the frequent changing of the solutions.

The effect of transplantation upon the metabolism of cartilage. Following implantation for 7 days a marked decrease in respiration and anaerobic glycolysis was noted in all of the grafts. Statistical analysis of the data from 7 to 150 days for the autografts and direct and frozen-dried homografts, however, revealed no further significant difference between the values for consecutive time periods. The results in each series were, therefore, grouped irrespective of the time that elapsed since implantation. The mean QO_2 was -0.23 ± 0.08 for the autografts, -0.22 ± 0.07 for the direct homografts, and -0.07 ± 0.03 for the frozen-dried homografts. The corresponding values for anaerobic glycolysis were $+0.46\pm0.12$, $+0.40\pm0.13$, and $+0.14\pm0.08$. Since the analysis of these three types of grafts indicated that the greatest change in metabolism occurred before the seventh day of implantation, the merthosaline preserved homografts were studied only for this period of time.

Comparison of the collective values revealed that there was no salient difference between the metabolic activity of the autografts and direct homografts (Table I). Each group showed approximately a 45 per cent decline in respiration and anaerobic glycolysis following transplantation. The preserved homografts, on the other hand, displayed no significant variation in their respiratory rate after transplantation, but seemed to show a slight increase in anaerobic activity (Table I). This increase could possibly be related to the function of soluble enzymes present in the tissue fluid which had infiltrated these grafts after transplantation. The respiratory enzymes, being insoluble and intimately associated with intracellular mitochondria, were, therefore, not increased.

Potter has indicated that tissue viability is dependent upon the function and spacial relationship of the cellular enzymes. The well defined values for respiration and anaerobic glycolysis recorded from the autografts and direct homografts are, therefore, indicative of the presence of living cartilage cells in these transplants. This substantiates the previous gross and histologic evidence that such grafts remain at least partially vital after transplantation. The decline in respiration and anaerobic glycolysis shown by these transplants could be partly attributed to a decrease in the number of viable chondrocytes resulting from the metabolic disturbances during transplantation as well as the trauma incident to the surgical manipulation of the tissues. The reduction in metabolism was so great, however, as also to implicate a decline in the metabolic activity of the remaining chondrocytes. The decrease in metabolism of these cells, though, was less than the data would seem to imply, since the values were based upon the total weight of the grafts rather than upon the viable cell content. The negligible changes in weight associated with cellular necrosis in a relatively acellular, firm tissue such as cartilage would thus be reflected as even further decreases in metabolic activity during computation of the QO_2 and $Q_G^N{}_2$ values.

Evaluation of preserved cartilage grafts. An evaluation of the frozen-dried homograft was included in this investigation because of the possibility of using this method for the storage of cadaver cartilage. Gersh has stated that tissue thus treated ". . . is without a doubt far closer to the living cell as regards the disposition and state of the solid constituents than can be obtained by any other method developed up to the present time." The extremely low metabolic activity recorded from the frozen-dried cartilage, nevertheless, indicated that few, if any, chondrocytes survived. A similar situation existed with the merthosaline preserved cartilage. That these values were not the result of an artefact, however, was substantiated by the failure to demonstrate respiration and anaerobic glycolysis in autoclaved cartilage. The reports of satisfactory clinical results with preserved grafts raise the question of whether viable cells are essential for the persistence of these transplants. It appears that the physical and chemical state of the matrix may be a governing factor. Additional histologic and clinical studies of frozen-dried and merthosaline preserved cartilage grafts are needed before a comparative evaluation

of these methods of preservation can be made.

Clinical application of the experimental results. Gross and histologic studies of the fate of various types of tissue transplants have shown that autogenous grafting can be successfully accomplished in many instances. Most homotransplants fail to survive, however, partially because of their inability to withstand the complicated cellular and immunologic response of the host. Loeb has indicated that this host reaction is due primarily to variations between the chemical constitution of certain substances elaborated by the graft, which he termed individuality differentials, and the tissue fluids of the recipient animal. In an autogenous environment, these factors produce no abnormal reaction. In homogenous surroundings, however, they act not only as toxins (homoiotoxins) which result in the local tissue reaction, but they also stimulate the formation of immune bodies which intensify this response. Loeb demonstrated that tissues with the most active metabolism produced these materials in the greatest quantity. It has been shown in this investigation that the metabolism of cartilage homografts is exceedingly low. The response of the host provoked by these grafts would, therefore, be minimal in comparison with that toward more energetic tissues. This offers a partial explanation for the favorable clinical results obtained with such transplants. Similar factors may also play a role in transplanted cornea, the metabolism of which closely resembles cartilage (Table II).

Cartilage, unlike most other tissues, exhibits a predominately anaerobic metabolism. It is, therefore, better able to withstand the hypoxic state during transplantation and in the period of adjustment thereafter. Being avascular, cartilage can also more readily reestablish its normal diffusion pattern with the surrounding tissue fluids. All of these factors, no doubt, contribute significantly to the maintenance of cartilage grafts.

SUMMARY

This investigation was concerned with the metabolic activity of fresh rabbit costal cartilage, preserved cartilage (frozen-dried, merthosaline), cartilage autografts, and fresh and preserved cartilage homografts. The respiration (QO_2) and anaerobic glycolysis ($Q^{N}_{G}2$) of each group were determined manometrically in the Warburg respirometer. The autografts, and fresh and frozen-dried homografts were studied at intervals of 7, 11, 15, 30, 60, 90, 120, and 150 days following implantation. The merthosaline homografts were analyzed after only 7 days. The metabolism of the cartilage transplants was compared with that of fresh and autoclaved costal cartilage from rabbits of similar age and weight as the donor animals, and with nontransplanted cartilage preserved by freezing and dehydration (−38 degrees C.) for 7 and 84 days or in merthosaline (5 degrees C.) for periods of 7, 21, 28, and 91 days. The following observations were made:

1. The rate of respiration and anaerobic glycolysis of fresh rabbit costal cartilage was among the lowest of all tissues. Carbohydrate metabolism was predominately anaerobic. No metabolic activity was recorded after the tissue was autoclaved.

2. During the first 7 days following transplantation, the rates of respiration and anaerobic glycolysis in both the autografts and direct homografts decreased to almost one-half that of fresh cartilage. After this initial decline, no further significant variations occurred in either series. The major portion of the metabolic activity remained on an anaerobic basis.

3. Cartilage preserved in merthosaline or by freezing-drying for 7 days exhibited only about one-fifth the normal rate of carbohydrate metabolism. Following implantation, these homografts showed no additional change in their rates of respiration, but revealed a slight increase in anaerobic activity.

4. Specimens preserved in the same merthosaline solution for periods longer than 7 days (14 and 28) did not show any further variation in respiration and anaerobic glycolysis. In the 91 day series, however, where the solution was changed 8 times, metabolic activity was completely abolished. Preservation in the freezing-drying apparatus for 84

days produced no additional decline in anaerobic glycolysis beyond that observed after 7 days, but oxygen consumption could no longer be demonstrated.

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EDITORIALS

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CARDIAC STANDSTILL

WHILE cardiac standstill in its legendary form aroused some incredulity, the modern version and its close relationship to medicine as a whole and to surgery in particular presents a problem of the first magnitude.

Increasing numbers of papers are appearing, presenting constantly longer series of cases, with methods of treatment and their results. With the various methods used, the recovery rates as reported have great variations—between 33 and 80 per cent. The rate of recovery depends perhaps more on the promptness with which adequate treatment is undertaken than on any other factor. This, of course, applies only to cases in which arrest has occurred in an otherwise fairly healthy heart and not in cases of late toxemia or death from other causes, in which cardiac standstill naturally occurs.

Modern methods of cardiac resuscitation may be applied with satisfactory results in many cases of drowning, accidental electrocution, strangulation, anoxia, poisoning from noxious fumes and gases, and they should be applied promptly in cases of arrest under anesthesia.

It is common knowledge that every anesthetic agent, if pushed beyond its therapeutic dosage, will cause death, preceded in many instances by cardiac standstill. It cannot be too strongly emphasized, therefore, that the responsibility rests largely on the anesthetist. With the exception of hemorrhage at operation, a disaster which has receded almost in proportion to the training of surgeons, there is little a surgeon can do in orthodox surgery that approaches in swiftness the possible fatal effect of improper anesthesia. The surgeon's errors usually begin groaning and moaning in a matter of hours, days, weeks, or years, but those of the anesthetist flash by like the crack of doom.

The heart is the toughest, strongest, most persistent, and tenacious organ and carries on and adapts itself against almost any odds, often for a time without support of other organs. When, therefore, under anesthesia standstill occurs, the heart has been tortured beyond these extremes. Direct contact with the heart by the surgeon may precipitate standstill, but only rarely in my experience. Considering how every anesthetist with every anesthetic administration enters the outer fringes of the cloud of death, I remain thankful that my lot has fallen in the less turbulent ways of surgery.

Too often in my experience with cardiac standstill has this urgent situation become a sudden and hair-raising discovery. It is contended that rarely, if ever, unless the heart is being handled, does standstill suddenly fall

like the stroke of doom on a smooth running and uneventful scene. If the anesthetist is sensitive and on the job, making acute and accurate observations at very short, perhaps half or quarter minute intervals, the impending disaster will make its insidious approach known by changes in blood pressure, pulse rate, respiratory phase and rate, sweating, color, eye changes, bleeding in the field, and when timely and life-saving measures may be undertaken. How often has the surgeon, busily engaged, becoming aware of less bleeding from tissues, alerted an inattentive anesthetist, who as a result of his investigations then announces, "The patient has no blood pressure." It is because of such incidents that I insist on half minute reports on the patient's condition, which tell me that the anesthetist is on the job.

If under well controlled conditions disaster is approaching, adjustments may turn the tide of events, or if the worst happens and standstill occurs immediate resuscitative methods can be instituted. The importance of prompt action is emphasized by reports which show that cardiac massage was successful with recovery in 85 per cent when undertaken within 5 minutes; if the interval was between 5 and 15 minutes the recovery rate fell to 33 per cent.

Reasonable consideration must be given the heart if it is being handled or operated upon. It must be remembered that the heart must have a rest period and be given time to fill between beats. If continuous trauma is applied, the heart responds by rapidly repeated contractions; as a result it is unable to empty itself, dilatation occurs, and soon cardiac standstill may appear, which will soon be replaced by fibrillation. The surgeon must therefore inflict what injury is necessary in short relays, so that the heart has a period to resume its normal function and poise.

In the presence of standstill, cardiac massage, 50 to 70 per minute, was first used by Nichaus in 1889, by Inelsand successfully in 1901, Starling and Lane in 1902, and subsequently by many others. Kountz was able to revive 65 of 127 hearts recovered 5 to 6 hours after death, showing that the heart may respond to treatment perhaps long after other organs, such as the brain and liver, have lost their power to regain function. When the heart has been emptied by massage, stimulation by 3 to 4 cubic centimeters of 10 per cent calcium chloride, epinephrine, isopropyl epinephrine, barium chloride, may initiate systole. Aortic or arterial transfusion should be prepared for and used. Electrical defibrillators may help in restoring systole and should be on hand and ready for use. If the chest is not open and there has been no response to drugs, it should be opened rapidly through the fourth left intercostal space, and for most efficient massage at 50 to 70 per minute the pericardium should be opened as well.

These efforts should produce a blood pressure of 50 to 80 millimeters of mercury, measurable by the anesthetist, and should continue for 60 to 80 minutes; beyond this time no recoveries have been reported.

GORDON MURRAY.

THE TEACHING OF MEDICAL HISTORY

NO living and growing society seems to remain satisfied for long with the education of its members. Therefore the fact that physicians are becoming increasingly critical of their educational background is encouraging.

Physicians realize that despite the giant strides made in therapy they still must treat patients and not diseases. Consequently knowledge of man's origins, social patterns,

and ideals must form the philosophical basis of medical practice. This is the reason that some of our finest doctors come from the group that trained in the liberal arts and subsequently decided to pursue the study of medicine.

Students who decide early in life to become doctors usually channel their studies along scientific lines while they are still in secondary school. They are impatient with every course that seems to them to have no direct bearing upon medicine. The humanities have little interest for them.

Because so many applicants present themselves to medical schools with this narrow outlook, the idea of required courses in the humanities as a prerequisite to entrance is being considered by many groups. Those who can recall their own attitudes as students will remember how onerous and unrewarding "required courses" can be made. Often the teacher comes to detest the teaching and the student to detest both the course and the teacher. So the addition of more required courses would seem to be of doubtful value because of the fact that the law of diminishing returns begins to operate early under such circumstances.

"The soul's incentive comes from within" and if the pursuit of learning can be made an avocation, the end will be already achieved. So the problem may be simply stated: how does one reach the receptive soul to fire this great emotional urge?

As a practical approach, offering an elective course in the History of Medicine to premedical students has seemed to bear fruit where it has been tried. The premedical student is still impressionable and all things medical are of great interest to him. His eagerness affords a rare opportunity for the right teacher. The long procession of great physicians from Imhotep on can be made to live again reflected against the background of their own civilizations. These great prototypes of the educated physician cannot help but inspire emulations if properly introduced.

A competent physician who loves the arts can obtain great satisfaction from teaching such a course to college students. Not only will he encourage many to broaden their training, but he may stimulate in a few a love for books that will continue to enrich their personal lives and practice and add luster to the tradition of the educated physician.

GEORGE A. COLLETT.

THE SURGEON AT WORK

A METHOD FOR SEGREGATION OF THE ENTIRE SMALL INTESTINE

FRANK H. LAHEY, M.D., F.A.C.S., Boston, Massachusetts

IN the course of many operations on the colon, for carcinoma, which require extensive removal of colon segments, or in the course of colectomies for ulcerative colitis involving the removal of all of the colon down to the sigmoid, I have often been greatly aided by complete evisceration of the small intestine. In doing this, I have been accustomed to eviscerate the small bowel into large, wet, warm pads of gauze. This method has not been completely satisfactory because loops of bowel escape from the pads, the pads become cool, and, furthermore, gauze is not the best material to have in contact with the delicate visceral peritoneum over a considerable period of time. For this reason I had two bags made, one large and one small (Fig. 1), one to receive the small intestine of a large adult and the other the small intestine of a thin, small adult or of a child. These bags have a double drawstring at the open end so that, with all of the intestine within the bag, the neck of the bag may be pulled together tightly enough to keep the intestine in place but not tightly enough to interfere in any way with the blood supply.

From the Department of Surgery, The Lahey Clinic, Boston.

With all of the small intestine segregated into such a bag with the neck drawn up, it may be hung either to the left or to the right of the abdominal incision, as desired, so that the colon or the stomach may be worked on from either side (Fig. 2).

This bag of easily stretchable rubber is smooth, and it is thick enough to hold heat within it. In any surgical condition in the abdomen that is not of an inflammatory character and not of a type that involves the small intestine, the use of this bag makes it possible to obtain operating conditions and exposures comparable with those conditions which would be obtained on a cadaver in which all of the small intestine had been removed.

These bags have now been employed a sufficient number of times so that one can say that they have many advantages and apparently no disadvantages. It is important to stress that the surgeon must be extremely careful in pulling the drawstrings up at the neck of the bag so that the neck is not closed so tightly as to produce constriction of the blood supply in the mesenteric roots of the bowel segregated in the bag. On the other hand, the drawstrings must be pulled to-

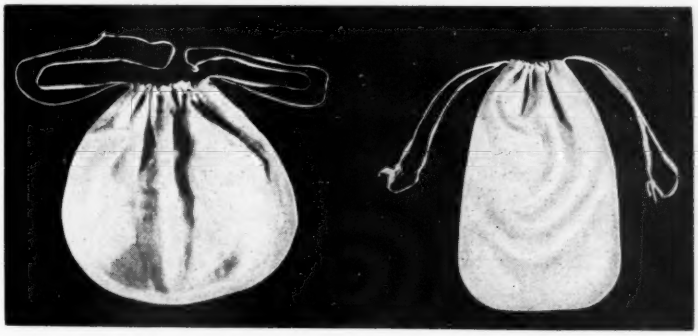

Fig. 1. These photographs illustrate the large and the small bag; the large for large adults with a large mass of small intestine, and the smaller bag for children and small adults.

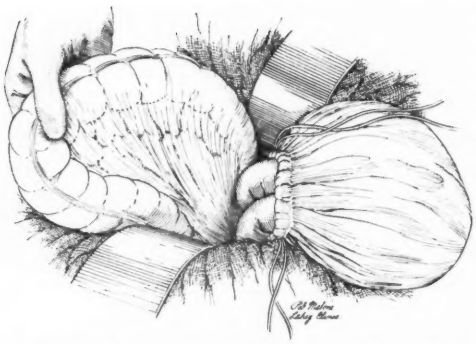

Fig. 2. This illustration shows how all of the small intestine from the jejunum to terminal ileum can be segregated into this rubber bag with the drawstring closed at the neck so that the colon can be worked on without the exposure being interfered with by the small intestine.

gether with reasonable tightness, or troublesome loops of small bowel will escape from the bag and perhaps interfere with the clearness of the field.

A simple way to get all of the small intestine into the bag is to grasp the mesenteric root of the small intestine within the abdomen in one hand, with the jejunum at one end of the grasped mesenteric root and the ileum at the other. They can all then be easily manipulated into the bag and the drawstring pulled up around the root of the mesentery.

This is a simple and apparently a safe method of obtaining the exposures which go with complete evisceration of the small intestine out of the abdomen without the disadvantages of heat loss and peritoneal irritation which accompany small intestinal evisceration without the use of such a bag.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

WE now have the final pages of the important work on roentgen diagnosis, *Lehrbuch der Roentgendiagnostik*[1]. It has appeared in eight parts, appearing at intervals during the last three years. The first four parts relate to the skeleton and have already been reviewed in these pages, as well as the next two parts on the chest. The two parts before us are devoted to the abdominal and pelvic organs.

The medical world owes a debt of gratitude to the authors of this excellent encyclopedic textbook on roentgenologic diagnosis. Consideration is given to the anatomic and physiologic aspects of the various organs as they relate to roentgenology, followed by the complete discussion of the pathologic phases. The present parts, 7 and 8, include the digestive tract, the urinary tract, and those phases of gynecology and obstetrics in which the roentgen aids to diagnosis play a part. As with the previous volumes, the discussion includes the anatomic and physiologic considerations, the etiology, pathology and roentgen findings, to which is added the use of the roentgen ray method in connection with, and after, surgery. Everywhere in the book the authors have been conscious of the relation of heredity to disease and have entered into much detail as to genetic considerations. The generous allotment to the digestive tract was written by W. E. Baensch of Georgetown University; the urinary tract by N. P. G. Edling of Sweden; and the gynecologic section by A. Zuppinger of Switzerland. The illustrations are beautifully done. With few exceptions they are in the "positive," thus preserving a greater percentage of detail than would have been the case had the illustrations been presented in the "negative." The experience of every radiologist in fluoroscopy, however, renders it immaterial to him whether the illustrations appear in the negative or in the positive.

This entire authoritative work, amounting to nearly 4,000 pages, constitutes a veritable monument to the industry of the authors and contributors. These volumes will surely be considered the most complete reference work on radiology. We are informed that the publication of the English edition will be completed during 1953.

There are two very full indexes in the set, one for the first four sections on the skeleton and one for the second four sections on the internal organs. Part 8 contains the author index for the entire work.

JAMES T. CASE.

[1]LEHRBUCH DER ROENTGENDIAGNOSTIK. Parts 7 and 8. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. Stuttgart: George Thieme; New York: Grune & Stratton, Inc., 1952.

ANY physician confronted with a puzzling case with multiple bone lesions can find the answer to his problem in Sir Thomas Fairbank's *Atlas of General Affections of the Skeleton*.[2] In fact Tables III, IV, V, and VI in the introduction provide an excellent guide for differential diagnosis or diagnosis by exclusion. The subsequent text amply supplies a complete description of each and every disorder, and chapter headings are replete with synonyms.

Adequate references are listed after each disease entity and followed by succinct case histories which are most informative. Extreme care has obviously been exercised to have the illustrations on the same page as the descriptive text. All these factors make for easy readability.

As the title implies, the book is abundantly provided with illustrations—510 in number. A few of these are photographs and photomicrographs but the majority are positive roentgenograms. Twelve negative roentgenograms crept in and do not mar the result but serve to support a slight preference for the negative type of roentgenographic reproduction.

This book contains all the skeletal conditions one hears about but seldom sees and many that some of us have never heard of. It is an excellent treatise and should have a wide field of usefulness.

NORMAN L. HIGINBOTHAM.

THE fourth edition of the important gynecological text by Emil and Edmund Novak[3] follows the eminently satisfactory pattern of the previous editions. The result is a well balanced, complete, and up-to-date textbook which is written in the authors' characteristic, easy, lucid style. The illustrations are well selected and handsomely reproduced. The pathology of gynecological disease is entirely authoritative, as befits one of our most distinguished gynecological pathologists, and is presented in sufficient detail to illustrate the bases of gynecological symptoms and diagnosis. The principles of therapy are outlined in detail and are presented in a practical and clear manner. As in previous editions, the indications, purposes, and scope of gynecological operative procedures are included, but the details of surgical technique are omitted. The text has been very carefully edited and contains

[2]AN ATLAS OF GENERAL AFFECTIONS OF THE SKELETON. By Sir Thomas Fairbank, D.S.O., O.B.E., M.S., Hon.M.Ch.(Orth.), F.R.C.S. Baltimore: The Williams & Wilkins Co., 1951.

[3]TEXTBOOK OF GYNECOLOGY. By Emil Novak, A.B., M.D., D.Sc. (Hon.), F.A.C.S., F.R.C.O.G. (Hon.), and Edmund R. Novak, A.B., M.D., F.A.C.S. 4th ed. Baltimore: The Williams & Wilkins Co., 1952.

many additions which bring it up to date. Among these, notable additions are made to the discussion of carcinoma in situ, the management of carcinoma of the cervix, hydatid mole, and functioning ovarian tumors. This is an outstanding text which in its new edition will continue to be of the greatest usefulness to medical students and practitioners alike.

D. N. DANFORTH.

A NOTEWORTHY contribution to medical letters is presented by R. W. Johnstone in his *William Smellie; the Master of British Midwifery*.[1] There has been a need for a new life of Smellie. The last one, written 60 years ago by Glaister, is out of print and relatively inaccessible. As a result, students and obstetricians are not as well acquainted as they might be with Smellie and his work. His immortal contributions to the development and science of midwifery form a fundamental part of their obstetrical training and practice.

Professor Johnstone, who is himself an eminent obstetrician, writes with a quiet elegance and charm that places his story apart from the usual medical biography. He has sketched William Smellie the man, the obstetrician, the teacher, and the writer with such warmth and clarity that the reader has little difficulty in envisaging the "big-handed Scotsman," who, without ever having belonged to the staff of a London Hospital and "never having delivered a Lady," yet compounded many of the fundamental principles of good obstetrical practice.

In a brief 136 pages the author portrays Smellie first as a young practitioner in a Scottish country town whose meticulously kept case histories give an insight into not only his character but also the condition of 18th century rural obstetrics. After Smellie's transfer to London, he carries him through the periods of his growth as a teacher, a clinician, and a creator of obstetrical theories and practices. After describing Smellie's return to Scotland, where during his remaining 3 years he completed his *Treatise* (edited, incidentally, by Tobias Smollett), the author presents two little known manuscript letters by Smellie. The last chapter, "Smellie's Greatness and Posthumous Fame," is a judicial evaluation of Smellie's character, of his contributions to midwifery, and of his right to a place among medical immortals.

The reader gains an excellent idea of Smellie's teachings from the quotations and illustrations from his *Treatise on the Theory and Practice of Midwifery*, his *Set of Anatomical Tables* and the biographer's comments on them, which form the substance of much of the book. Inevitably, Smellie, as a revolutionist of obstetrical practices at a time when men midwives were still in an equivocal position, was to run afoul of his contemporaries. The attacks and criticisms which were made upon him and his reluctance to reply in kind are mentioned.

The book belongs on the obstetricians' reading table and in the doctors' and interns' room of every maternity ward. It is enjoyable reading, it is good obstetrics, and it is a worthy memorial to a great man.

JOHN W. HUFFMAN.

IN the preface to *Neurosurgery in General Practice* by Adrian Ver Bruggen[2] it is stated that the purpose of this book is to help the general practitioner with his neurosurgical problems. Some patients, who may later pass into the hands of the neurosurgeons, are stricken suddenly and the family doctor is the first to see him and treat him. How should he proceed? Others present themselves with less acute conditions involving the nervous system in which there is a possibility of successful neurosurgical intervention. How can these particular neurosurgical problems be recognized? The answers to these questions are provided in this volume.

This volume is designed primarily to help the general practitioner to decide whether a patient presents a neurosurgical problem, and if so, to help him make an early proper disposition of the neurosurgical case. No attempt is made to teach neurosurgery as it would be taught to a neurosurgeon, nor to teach operative neurosurgery. It does give a clear and concise exposition of neurosurgery, as the general practitioner should know it, and how to proceed with neurosurgical problems. It is my feeling that the author has done an admirable job in presenting what is generally regarded as good, sound neurosurgical opinion. Purely personal views are avoided in this book.

This volume will interest not only the general practitioner of medicine, but should be extremely valuable to the medical student, the neuropsychiatrist, the pediatrician, and the diagnostician.

There are 26 chapters, all well written, and generously illustrated with excellent black and white photographs. At the conclusion of each chapter, there are several illustrative cases, in which brief histories, and physical findings are given to illustrate the problems enumerated in each individual chapter. The first 5 chapters deal with head injuries, injuries to the cranial bones, extradural hemorrhage, chronic subdural hematoma, and head injuries in children. It will be noted that references and bibliography are not extensive; they have been selected as far as possible with a view to availability and completeness. The chapters that deal with peripheral nerve injuries and with the cerebellar tumors in children are particularly outstanding. Automobile accidents lead to the severing of nerves, especially at the wrist and forearm, and the general practitioner is often called upon to close these wounds in which a severed nerve is often seen. An early anastomosis of the nerve ends may often be done. In other cases of peripheral nerve injury, primary closure of the wound may be done without

[1] WILLIAM SMELLIE; THE MASTER OF BRITISH MIDWIFERY. By R. W. Johnstone, C.B.E., M.A., M.D., Hon. LL.D. Edinburgh and London: E. & S. Livingstone, Ltd., 1952.

[2] NEUROSURGERY IN GENERAL PRACTICE. By Adrien Ver Brugghen, M.B., Ch.M., M.S., F.A.C.S. Springfield, Ill.: Charles C Thomas, 1952.

any attempt to approximate the ends of the severed nerve. This remains to be done at a later date, but the optimum time must be selected. It is usually possible from the anatomical position of the injury to form an idea which nerve or nerves may be implicated, and motor and sensory tests should be carried out before any treatment is undertaken. The author discusses nonoperative treatment of peripheral nerve injuries, primary nerve suture, secondary repair of peripheral nerves, and methods of determining recovery of function.

In the chapter on cerebral vascular diseases, the author discusses an interesting therapeutic application on the principle of position in the treatment of a patient with a leaking intracranial aneurysm. The leaking vessel lies between the brain above and the floor of the skull or tentorium below. By keeping the patient sitting up throughout his stay in the hospital, it is believed that the brain may be brought in contact with the open vessel and tamponaded. The brain in contact with the aneurysmal sac may seal it off.

One chapter is devoted entirely to spinal puncture, and the author is to be commended for clarifying much of the misunderstanding that still exists about the advantages and disadvantages of this very simple and supposedly standardized procedure. It is commonplace for interns, residents, general practitioners, and diagnosticians to do spinal fluid studies with Queckenstedt maneuvers on people with increased intracranial pressure. The Queckenstedt test is of course helpful in testing for spinal block, but it rarely is of help in diagnosing intracranial lesions, with the possible exception of the possibility of a cavernous sinus thrombosis, and under no circumstances should jugular pressure be applied in cases of increased intracranial pressure. Spinal puncture should not be done on patients with spinal fluid leaks, especially those associated with skull fracture. The withdrawal of fluid through the needle may reverse the flow of fluid which is escaping from the ear or nose. Though this is only temporary, fluid may return to the subarachnoid space which has been in contact with unsterile external tissues. In the case of the nose, the tissue may be laden with bacteria.

In Chapter 25, some common x-ray findings connected with roentgen examination of the skull are included. Mention is made of certain x-ray changes, not considered to be of localizing value, for they occur equally well when the pressure symptoms originate from the lesion above or below the tentorium. These changes are: first, erosion of the posterior clinoid processes; second, erosion of the floor of the sella turcica; third, increased convolutional markings; and fourth, separations of the sutures in children. Ballooning of the sella turcica, calcified lesions within the cranium, hyperostosis, rarefaction of bone, and changes in the pineal gland are all readily demonstrable in the routine x-rays of the skull. A discussion follows on the indications and technical aspects of performing encephalography and ventriculography. The author also includes in the chapter on x-ray diagnosis, several excellent photographs and discussions on the value of cerebral angiography.

This volume is a most worthwhile treatise on neurosurgery in general practice. The scope of the subject matter, the written test, the illustrations, are all very well done, and the book has much to offer to the general practitioner, as well as physicians in other branches of medicine and surgery.

HOWARD H. LANDER.

IN Volume IV of his admirable and well illustrated *Post-Graduate Lectures on Orthopedic Diagnosis and Indications*[1] Steindler discusses, in Section A, the problems of arthritis, spondyloarthritis, gout, pyogenic arthritis, syphilis of bones and joints, inflammatory diseases of muscles, diseases of tendons and bursae, and muscular dystrophy and atrophy. In Section B are considered deficiency and degenerative diseases of bones and joints.

A little more than one half of this 300 page volume is devoted to the important problem of arthritis with its 7,000,000 victims. ("It is claimed that in this country almost 7,000,000 people suffer from either atrophic or hypertropic arthritis or from muscular rheumatism" p. 19.) Both the difficulty of the problem and the author's approach to it are indicated in an early paragraph, "One can never arrive at a proper concept of nonspecific arthritis if one looks at it merely in the light of the invader. It is at least of equal importance to investigate the reasons why a particular individual is or may become susceptible to the disease. Quite obviously there must exist a general immunity against arthritis, whatever its cause may be, for the simple reason that the causes are ubiquitous, and the disease is selective. . . . Let us take, for instance, the case of arthritis caused by infection of the upper air passages such as the tonsils or sinuses. The incidence of these infections in the human race is infinitely greater than is the incidence of arthritis, which is supposed to be caused by these infections. The inescapable conclusion therefore is that in addition to an external agent of infectious, metabolic, endocrine, or even mechanical nature a constitutional susceptibility or weakness is necessary to produce the arthritis."

In very direct and clear cut fashion Steindler takes up with each major subject the questions of etiology, pathological change, clinical, and x-ray findings, and treatment. In weighing the results of surgical treatment he attempts, as in all his contributions, to estimate objectively the results in percentages of good results, fair, and poor. Another exceedingly helpful feature of Steindler's lectures is his frequent reference to the work of others, and the list of references given at the end of each lecture.

[1] POST-GRADUATE LECTURES ON ORTHOPEDIC DIAGNOSIS AND INDICATIONS. By Arthur Steindler, M.D., F.A.C.S. Vol. 4. Section A: ARTHRITIS AND DISEASES OF MUSCLES, BURSAE, TENDONS, AND FASCIAE. Section B: DEFICIENCY AND DEGENERATIVE DISEASES OF THE LOCOMOTOR SYSTEM. Springfield, Ill.: Charles C Thomas, 1952.

The student who would go further into any of the problems that the author has taken up in this broad survey can find definite directions to guide him along the way. SUMNER L. KOCH.

THE author of *Lumbar Disc Lesions*,[1] J. R. Armstrong, has had a wide experience in dealing with the lumbago sciatica problem and has set down his views in his book. His approach is a fair representation of the way in which most orthopedic surgeons in the British Isles deal with what Osmond-Clark in his foreword calls "this often recalcitrant problem."

The layout and illustrations are good, and the problem, its anatomy, its pathogenesis, elucidation, and treatment are considered in orderly detail. The use of myelography is limited to those patients suspected of having a spinal tumor. Mr. Armstrong also routinely explores the lower two lumbar discs. Both these measures are now generally acknowledged to be sound practice, and most surgeons will join with the author in his condemnation of manipulative treatment.

It is unfortunate that Mr. Armstrong has given us no detailed analysis of his large series of over a thousand operations. Also it is surprising to see the "H" graft advocated in spinal fusion when in most hands this technique has shown a rather high incidence of pseudarthrosis formation. These, however, are minor criticisms of a well written and excellent monograph which can be recommended to all who have to deal with this common complaint.

HAROLD BOLTON.

[1] LUMBAR DISC LESIONS; PATHOGENESIS AND TREATMENT OF LOW BACK PAIN AND SCIATICA. By J. R. Armstrong, M.D., M.Ch., F.R.C.S. Edinburgh, London: E. & S. Livingstone, Ltd.; Baltimore: The Williams & Wilkins Co., 1952.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

OBSTETRICIA PRACTICA VERSION. By Juan Leon. Buenos Aires: Libreria "El Ateneo" Editorial, 1952.

CIRURGIA DO RIM EM FERRANDURA. By Dr. Octacilio Gualberto de Oliveira. Rio de Janeiro: Revista Brasileira de Cirurgia, 1950.

TASCHENBUCH DER PRAKTISCHEN MEDIZIN. Compiled by various authors. Edited by Dr. J. Kottmaier. 2nd rev. ed. Stuttgart: Georg Thieme, 1953.

SYNOVIAL FLUID CHANGES IN JOINT DISEASE. By Marian W. Ropes, M.D., and Walter Bauer, M.D. Cambridge, Mass.: Published for The Commonwealth Fund by Harvard University Press, 1953.

COMMOTIO CEREBRI; CEREBRAL CONCUSSION AND THE POSTCONCUSSION SYNDROME IN THEIR MEDICAL AND LEGAL ASPECTS. By Cyril B. Courville, M.D. Los Angeles: San Lucas Press, 1953.

ENDOCRINE TREATMENT IN GENERAL PRACTICE. Edited by Max A. Goldzieher, M.D., and Joseph W. Goldzieher, M.D. New York: Springer Publishing Co., Inc., 1953.

FUNDAMENTALS OF CLINICAL CANCER; WITH EMPHASIS ON EARLY DIAGNOSIS AND TREATMENT. By Leonard B. Goldman, M.D. New York: Grune & Stratton, 1953.

DIE KONSERVIERUNG VON KNOCHENGEWEBE FÜR TRANSPLANTATIONEN. By Hans Roth. Wien: Springer-Verlag, 1952.

AMERICAN POCKET MEDICAL DICTIONARY; A DICTIONARY OF THE PRINCIPAL TERMS USED IN MEDICINE, NURSING, PHARMACY, DENTISTRY, VETERINARY SCIENCE, AND ALLIED BIOLOGICAL SUBJECTS. 19th ed. Philadelphia, London: W. B. Saunders Co., 1953.

GIFFORD'S TEXTBOOK OF OPHTHALMOLOGY. By Francis Heed Adler, M.D. 5th ed. Philadelphia, London: W. B. Saunders Co., 1953.

TREATMENT OF MENTAL DISORDER. By Leo Alexander, M.D. Philadelphia and London: W. B. Saunders Co., 1953.

FUNDAMENTALS OF CLINICAL ORTHOPEDICS. By Peter A. Casagrande, M.D., and Harold M. Frost, Jr., M.D. Forewords by Joseph S. Barr, M.D., and Frank N. Potts, M.D. New York: Grune & Stratton, 1953.

THE PHARYNX; BASIC ASPECTS AND CLINICAL PROBLEMS. Edited by Abraham R. Hollender, M.D., F.A.C.S. Chicago: The Year Book Publishers, Inc., 1953.

THE ANATOMY OF THE NERVOUS SYSTEM; ITS DEVELOPMENT AND FUNCTION. By Stephen Walter Ranson, M.D., Ph.D. Revised by Sam Lillard Clark, M.D., Ph.D. 9th ed. Philadelphia, London: W. B. Saunders Co., 1953.

A MANUAL OF CLINICAL ALLERGY. By John M. Sheldon, M.D., Robert G. Lovell, M.D., and Kenneth P. Mathews, M.D. Philadelphia, London: W. B. Saunders Co., 1953.

ERGEBNISSE DER GESAMTEN TUBERKULOSEFORSCHUNG. Edited by H. Beitzke, St. Engel, L. Heilmeyer, and J. Hein. Vol. 2. Stuttgart: Georg Thieme, 1953.

GASTRIC CANCER. By Alfred H. Iason. New York: Grune & Stratton, 1953.

THE PRINCIPLES OF NEUROLOGICAL SURGERY. By Loyal Davis, M.S., M.D., Ph.D., D.Sc., (Hon.). 4th rev. ed. Philadelphia: Lea & Febiger, 1953.

AN ATLAS OF SKULL ROENTGENOGRAMS. By Bernard S. Epstein, M.D., and Leo M. Davidoff, M.D. Philadelphia: Lea & Febiger, 1953.